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L1              0 S 5G1 1
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L7              0 S 5G325## OR 5G325##/AB
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L9              0 S (5G 46# OR 5G 27 OR 5G 27K OR 5G 200## )/AB
L10          2831 S GLOMERULONEPHRITI? OR NEPHRITIS?
L11          3132 S C5
L12             7 S L10 AND L11
L13         18194 S KIDNEY (L)  (DISEASE OR DISORDER#)
L14             7 S L13 AND L11
L15             9 S L14 OR L12
L16             0 S (5 G1 OR C5 G1 OR C5G1 OR 5G11 OR 5 G1 1 OR C5 G1 1)
L17            17 S (5 G1 OR C5 G1 OR C5G1 OR 5G11 OR 5 G1 1 OR C5 G1 1)/AB
L18             7 S L17 AND (MONOCLONAL# OR COMPLEMENT OR L11)
L19          8285 S ALPHA (L) CHAIN#
L20             8 S L11 (L) L19
L21             1 S L20 AND ANTIBOD?

     FILE 'HCA' ENTERED AT 10:19:45 ON 29 JUN 95

=> d bib abs hitind l15 1-9

L15  ANSWER 1 OF 9  HCA  COPYRIGHT 1995 ACS
AN   119:178954  HCA
TI   Nucleotide sequence of a human autoantibody to the alternative
     pathway C3/C5 convertase (C3NeF)
AU   Victor, Kimberly D.; Pascual, Virginia; Stitzel, Ann E.; Tsokos,
```

George C.; Capra, J. Donald; Spitzer, Roger E.
CS Southwest. Med. Cent., Univ. Texas, Dallas, TX, 75235-9048, USA
SO Hybridoma (1993), 12(3), 231-7
CODEN: HYBRDY; ISSN: 0272-457X
DT Journal
LA English
AB The prodn. of autoantibodies to the alternative pathway C3/C5 convertase or C3 Nephritic Factor (C3NeF) is one characteristic of membranoproliferative glomerulonephritis. The complete nucleotide sequences of the heavy and light chain variable regions of an IgGC3NeF produced by an EBV transformed B cell line derived from a patient with membranoproliferative glomerulonephritis were detd. The VH and VL gene segments used by this C3NeF are extensively mutated suggesting that antigenic selection and affinity maturation may occur during the generation of this autoantibodies.
CC 15-3 (Immunochemistry)
Section cross-reference(s): 3
IT Protein sequences
(for complement C3 nephritic factor, of humans with membranoproliferative **glomerulonephritis**)
IT Deoxyribonucleic acid sequences
(complementary, for complement C3 nephritic factor, of humans with membranoproliferative **glomerulonephritis**)
IT **Kidney, disease**
(membranoproliferative **glomerulonephritis**, complement C3 nephritic factor in humans with, sequence of)
IT 80342-06-9, Complement C3 nephritic factor
(amino acid and nucleotide sequence of, of humans with membranoproliferative **glomerulonephritis**)

L15 ANSWER 2 OF 9 HCA COPYRIGHT 1995 ACS
AN 117:5874 HCA
TI Significance and mechanism of glomerular C3d deposition in minimal change nephrotic syndrome (MCNS)
AU Endo, Morito; Ohi, Hiroyuki; Hatano, Michinobu
CS Sch. Med., Nihon Univ., Tokyo, 173, Japan
SO Nichidai Igaku Zasshi (1992), 51(1), 47-54
CODEN: NICHAS; ISSN: 0029-0424
DT Journal
LA Japanese
AB Clinicopathol. study was performed on renal biopsy specimens from 22 minimal change nephrotic syndrome patients (MCNS) to investigate the role of the complement system in the pathogenesis of MCNS. Complement C3d (C3d) fragment, a breakdown product of C3, was detected without Igs or complement C3c fragment in 14 cases out of the 22 MCNS patents. C3d deposits were usually obsd. in the capillary membrane and the mesangium. The patients with C3d deposits (14 cases) revealed no substantial differences from the patients without C3d deposits (8 cases) in their clin. features.

The renal biopsy specimen with C3d deposits were, however, obtained early during the onset of nephrotic syndrome and C3d displayed an ability for unique binding to the glomeruli.

CC 15-8 (Immunochemistry)
Section cross-reference(s): 14

IT **Kidney, disease**
(nephrotic syndrome, minimal-change, complement C3d deposition in glomerulus in, in human)

IT 60-27-5, Creatinine 80295-41-6, Complement C 3 80295-48-3, Complement C4 80295-53-0, Complement **C5** 80804-53-1, Complement iC3b
(of blood serum, in minimal-change nephrotic syndrome, complement C3d deposition in glomerulus in relation to, in human)

L15 ANSWER 3 OF 9 HCA COPYRIGHT 1995 ACS
AN 111:192889 HCA
TI Renal injury in DOCA-salt hypertensive **C5**-sufficient and **C5**-deficient mice
AU Raij, Leopoldo; Dalmasso, Agustin P.; Staley, Nancy A.; Fish, Alfred J.
CS Med. Sch., Univ. Minnesota, Minneapolis, MN, USA
SO Kidney Int. (1989), 36(4), 582-92
CODEN: KDYIA5; ISSN: 0085-2538
DT Journal
LA English
AB Hypertension was induced by uninephrectomy and treatment with desoxycorticosterone (DOCA) and 1% NaCl in the drinking water in congenic mice that differ in the single gene locus responsible for the presence of absence of the complement component C5. These mice were compared to uninephrectomized normotensive (no DOCA-NaCl) mice. In contrast to C5-sufficient (C5S) mice, C5-deficient (C5D) mice can neither generate C5a nor assemble C5b-9. After four weeks of treatment, DOCA-C5S and -C5D mice developed similar degrees of hypertension; mice receiving no DOCA remained normotensive. Only hypertensive mice developed glomerular injury. Hypertensive DOCA-C5D mice developed more glomerular capillary loop dilatation and larger glomerular capillary tuft vols. than DOCA-C5S mice. However, DOCA-C5S mice, compared to DOCA-C5D mice, had significantly more glomerular cell proliferation, cell necrosis, extracapillary proliferation, and proteinurea. By immunofluorescence microscopy both DOCA-C5S and -C5D had mesangial C3 deposits but only DOCA-C5S mice had C9 deposits. After 16 wk of DOCA-NaCl C5S mice, in comparison to C5D mice, had more severe glomerulosclerosis, proteinurea, and renal insufficiency. These changes occurred despite levels of hypertension that were similar in DOCA-NaCl C5S and C5D throughout the whole study period. C5a and/or C5b-9 may play an important role in hypertensive glomerular injury. Moreover, differences in host responses may det. target organ susceptibility to similar injurious mechanisms.

CC 15-8 (Immunochemistry)
IT **Kidney, disease** or **disorder**
(glomerulus, injury, in hypertension, complement C5a and C5b-9 role in)

L15 ANSWER 4 OF 9 HCA COPYRIGHT 1995 ACS
AN 106:117810 HCA
TI Effect of the anticomplementary agent, K-76 monocarboxylic acid, on experimental immune complex **glomerulonephritis** in rats
AU Iida, H.; Izumino, K.; Asaka, M.; Takata, M.; Mizumura, Y.; Sasayama, S.
CS Fac. Med., Toyama Med. Pharm. Univ., Toyama, Japan
SO Clin. Exp. Immunol. (1987), 67(1), 130-4
CODEN: CEXIAL; ISSN: 0009-9104
DT Journal
LA English
AB The authors examd. the effect of the anticomplementary agent K-76 monocarboxylic acid (K-76COOH), which is known to inhibit complement C5 activity, on immune complex glomerulonephritis in rats. Bovine serum albumin (BSA) nephritis was induced in rats by s.c. immunization and daily i.v. administration of BSA. K-76COOH (30 mg/kg) was administered i.p. twice daily for 4 wk. K-76COOH significantly reduced the development of proteinuria in the early stage of BSA nephritis, but it failed to suppress proteinuria in the late stage. There was no significant difference in glomerular changes between treated animals and non-treated controls. Apparently, C5 and the terminal complement components may play a significant role in protein excretion in the early stage of immune complex glomerulonephritis.
CC 15-4 (Immunochemistry)
ST complement **C5** immune complex **glomerulonephritis**; K76 carboxylate complement inhibition **glomerulonephritis**
IT Complement
(terminal components of, protein excretion in immune complex **glomerulonephritis** regulation by)
IT **Kidney, disease** or **disorder**
(immune complex **glomerulonephritis**, proteinuria in, complement **C5** and terminal complement complex regulation of)
IT Proteins, biological studies
(metabolic disorders, proteinuria, complement **C5** and terminal complement complex regulation of, in immune complex **glomerulonephritis**)
IT 88195-80-6
(complement **C5** inhibition by, in immune complex **glomerulonephritis**)
IT 80295-53-0, Complement **C5**
(protein excretion in immune complex **glomerulonephritis** regulation by)

L15 ANSWER 5 OF 9 HCA COPYRIGHT 1995 ACS
AN 95:224844 HCA
TI Organic solvents and chronic **glomerulonephritis**: a cross-sectional study with negative findings for aliphatic and alicyclic **C5**-C7 hydrocarbons
AU Mutti, A.; Lucertini, S.; Falzoi, M.; Cavatorta, A.; Franchini, I.
CS Ist. Semeiotica Med., Univ. Studi Parma, Parma, 43100, Italy
SO JAT, J. Appl. Toxicol. (1981), 1(4), 224-6
CODEN: JJATDK
DT Journal
LA English
AB Total protein excretion in workers exposed to org. solvents including C5-7 hydrocarbon mixts. is 60.3 .+-. 1.6% in workers with previous exposure, 54.8 .+-. 4.6; and in the control group, 48.3 .+-. 3.1 mg proteinuria/g creatinine.
CC 59-3 (Air Pollution and Industrial Hygiene)
ST org solvents proteinuria occupational exposure; **glomerulonephritis** org solvent occupational exposure
IT Hydrocarbons, biological studies
(**C5**-7, occupational exposure to, proteinuria in relation to)

L15 ANSWER 6 OF 9 HCA COPYRIGHT 1995 ACS
AN 88:187544 HCA
TI Observations on the evolution of idiopathic rapidly progressive **glomerulonephritis**
AU Davis, C. A.; McEnery, P. T.; Maby, S.; McAdams, A. J.; West, C. D.
CS Child. Hosp. Res. Found., Cincinnati, Ohio, USA
SO Clin. Nephrol. (1978), 9(3), 91-102
CODEN: CLNHBI; ISSN: 0301-0430
DT Journal
LA English
AB Deposits of C3, C5 and properdin were identified in the minimally proliferative glomerular lesions of a patient with idiopathic rapidly progressive glomerulonephritis. Biopsies of the renal allograft at times of recurrences of the disease and of five other patients with progressive renal failure but less severe crescent formation showed deposits identical in compn. and position. The deposits were subepithelial and located in that part of the basement membrane in apposition to the mesangium (capillary waist). The evidence indicated that all six patients were in early or late stages of idiopathic (nonstreptococcal) rapidly progressive glomerulonephritis.
CC 14-4 (Mammalian Pathological Biochemistry)
ST **glomerulonephritis** complement properdin glomerulus
IT Properdins
(of glomerular lesion in **glomerulonephritis**)
IT Complement

(C3, of glomerular lesion in **glomerulonephritis**)
IT Complement
(**C5**, of glomerular lesion in **glomerulonephritis**
)
IT **Kidney**, **disease** or **disorder**
(**glomerulonephritis**, complement and properdin of glomerular lesions in)

L15 ANSWER 7 OF 9 HCA COPYRIGHT 1995 ACS
AN 86:187493 HCA
TI Metabolism of the fifth component of complement, and its relation to metabolism of the third component, in patients with complement activation
AU Sissons, J. G. P.; Liebowitch, J.; Amos, N.; Peters, D. K.
CS Dep. Med., R. Postgrad. Med. Sch., London, Engl.
SO J. Clin. Invest. (1977), 59(4), 704-15
CODEN: JCINAO
DT Journal
LA English
AB The metab. of the 5th component of complement (C5), and its relation to metab. of C3, was studied in normal subjects and patients by simultaneous administration of I-labeled C5 (125I) and C3 (131I). In 7 normal subjects the fractional catabolic rate of C5 was 1.5-2.1% of the plasma pool/h and extravascular/intravascular distribution ratio from 0.22-0.78, these values being similar to those obtained for C3, and synthesis rate from 71-134 .mu.g/kg/h. In patients with complement activation the increase in fractional catabolic rate of C5 was usually less than C3. There was increased extravascular distribution of C3 and C5 in most patients and considerable extravascular catabolism of both proteins in some. However, there were differences in metabolic parameters between patients with different types of complement activation. In patients with systemic lupus erythematosus, fractional catabolism and extravascular distribution of C3 and C5 were both increased, and there was marked extravascular catabolism of both proteins. There was increased fractional catabolism and extravascular distribution of C3 in patients with mesangiocapillary nephritis and(or) partial lipodystrophy, and fractional catabolism of C5 was also increased in 3 of 6 studies although distribution of C5 was always within the normal range; however, in 2 patients with nephritic factor in their serum, fractional catabolism of C5 was normal despite markedly increased C3 turnover, suggesting that in patients with alternative pathway activation by nephritic factor little or no C5 convertase is generated.
CC 15-13 (Immunochemistry)
IT Lupus erythematosus
(complement C3 and **C5** metab. in)
IT Lipids
(metabolic disorders of, lipidystrophy, complement C3 and

C5 metab. in)
IT Complement
(**C5**, metab. of, in complement activation disorders, C3 in relation to)
IT **Kidney**, **disease** or **disorder**
(mesangiocapillary **nephritis**, complement C3 and **C5** metab. in)
IT **Kidney**, **disease** or **disorder**
(**nephritis**, complement C3 and **C5** metab. in)

L15 ANSWER 8 OF 9 HCA COPYRIGHT 1995 ACS
AN 83:76624 HCA
TI Complement components C3, **C5**, C6, C7, C8, and C9 in chronic membranoproliferative **glomerulonephritis**, systemic lupus erythematosus, poststreptococcal **nephritis**, idiopathic nephrotic syndrome, and anaphylactoid purpura
AU Geiger, Hartmut; Good, Robert A.; Day, Noorbibi K.
CS Univ.-Kinderklin. Heidelberg, Heidelberg, Ger.
SO Z. Kinderheilkd. (1975), 119(4), 269-78
CODEN: ZEKIA5
DT Journal
LA English
AB In a comparative study the hemolytic activity of C3, C5, C6, C7, C8, C9 and the C3 proactivator (C3PA) were measured in serums of 22 patients with chronic membranoproliferative glomerulonephritis (CMPGN), 15 patients with idiopathic nephrotic syndrome, 10 patients with systemic lupus erythematosus, 7 patients with anaphylactoid purpura and 10 patients with acute poststreptococcal nephritis. In CMPGN, C3, C5, C6, C7 and C8 were low in the majority of the patients, whereas C9 and C3PA were depressed only in 21% and 11% of the patients, resp. C3PA and C8 showed striking depressions in idiopathic nephrotic syndrome. In lupus erythematosus, all the C factors, including C3Pa were low with the exception of C9, which was normal in 80% of the patients studied. C3, C5, C6 and C7 were depressed in acute glomerulonephritis; C8 and C9 titers were normal. In all patients studied with anaphylactoid purpura, total hemolytic complement and C3 titers were elevated markedly.
CC 14-4 (Mammalian Pathological Biochemistry)
ST complement **nephritis** lupus purpura; **glomerulonephritis** complement fraction; lupus erythematosus complement fraction; **nephritis** complement fraction; nephrosis complement fraction; purpura complement fraction
IT Complement
(C3 and **C5** to C9, in blood serum in hepatopathy and lupus and purpura)
IT **Kidney**, **disease** or **disorder**
(**nephritis** and nephrosis, complement components of blood serum in)

L15 ANSWER 9 OF 9 HCA COPYRIGHT 1995 ACS
AN 74:109749 HCA
TI Role of **C5** in the **nephritis** of NZB/W mice
AU Lanier, B. G.; McDuffie, F. C.; Holley, K. E.
CS Dep. Med., Mayo Clin. and Mayo Found., Rochester, Minn., USA
SO J. Immunol. (1971), 106(3), 740-6
CODEN: JOIMA3
DT Journal
LA English
AB To det. the role of C5 in the spontaneous development of "autoimmune" nephritis in NZB/W mice, the F2 generation was produced and grouped according to C5 status by serum levels as detd. by radial immunodiffusion, i.e., homozygous negative (cc), heterozygous (Cc) and homozygous positive (CC). In both males and females, the frequency of nephritis was actually higher in mice lacking C5 (cc). When the figures for males and females were combined this difference was statistically significant. Thus, C5 does not contribute to the renal lesons of NZB/W mice. It may play some protective role, perhaps through some as yet unidentified anti-viral effect.
CC 13 (Immunochemistry)
IT Complement
(C'5, autoimmune **nephritis** in relation to)
IT Kidneys, diseases or disorders
(autoimmune **nephritis**, complement C'5 in relation to)

=> d bib abs hitind l18 1-7

L18 ANSWER 1 OF 7 HCA COPYRIGHT 1995 ACS
AN 122:23468 HCA
TI Selective inhibition of platelet macroaggregate formation by a recombinant heparin-binding domain of human thrombospondin
AU Legrand, Chantal; Morandi, Veronica; Mendelovitz, Simona; Shaked, Hadassa; Hartman, Jacob R.; Panet, Amos
CS Hopital St Louis, Paris, 75010, Fr.
SO Arterioscler. Thromb. (1994), 14(11), 1784-91
CODEN: ARTTE5; ISSN: 1049-8834
DT Journal
LA English
AB Thrombospondin (TSP) is a platelet .alpha.-granule adhesive protein that plays a crit. role in the stabilization of thrombus by promoting the formation of platelet macroaggregates. We have recently shown that a monoclonal antibody (mAb) to the NH2-terminal heparin-binding domain of TSP, MAII, inhibits platelet aggregation induced by thrombin in a dose-dependent manner. In this study, we have expressed in Escherichia coli two recombinant proteins comprising residues 1 to 174 (TSP18) and 1 to 242 (TSP28) of TSP. After purifn., both proteins reacted equally well with mAb MAII, whereas the reactivity of TSP18 for heparin was lower than that of TSP28 or native TSP. At micromolar concns., TSP18 and TSP28

inhibited the second wave of platelet aggregation and the concomitant release of [14C]5-hydroxytryptamine induced by ADP in citrated platelet-rich plasma as well as aggregation and secretion induced by a low concn. of thrombin in washed platelet suspensions. The proteins did not inhibit surface expression of endogenous TSP on activated platelets, as measured by the binding of radiolabeled mAb **5G11**, indicating that they did not interfere with the primary binding of TSP to the plasma membrane. In contrast, in a solid-phase binding assay, the proteins inhibited in a dose-dependent manner (IC50, 0.1 and 0.06 .mu.mol/L for TSP18 and TSP28, resp.) the binding of radiolabeled TSP to surface-adsorbed fibrinogen. Furthermore, specific and saturable binding of the proteins to immobilized fibrinogen was demonstrated by ELISA. The results suggest that interaction between the heparin-binding domain of TSP and membrane-bound fibrinogen may be crit. in the platelet aggregation/secretion process.

CC 1-8 (Pharmacology)
Section cross-reference(s): 13

IT Antibodies
(**monoclonal**, to heparin-binding domain of human thrombospondin; selective inhibition of platelet macroaggregate formation by a recombinant heparin-binding domain of human thrombospondin)

L18 ANSWER 2 OF 7 HCA COPYRIGHT 1995 ACS
AN 120:6430 HCA
TI A 29K envelope glycoprotein of equine arteritis virus expresses neutralization determinants recognized by murine **monoclonal** antibodies
AU Balasuriya, Udeni B. R.; Rossitto, Paul V.; DeMaula, Christopher D.; MacLachlan, N. James
CS Sch. Vet. Med., Univ. California, Davis, CA, 95616, USA
SO J. Gen. Virol. (1993), 74(11), 2525-9
CODEN: JGVIAY; ISSN: 0022-1317
DT Journal
LA English
AB A panel of 6 neutralizing murine monoclonal antibodies (MAbs) to equine arteritis virus (EAV) was produced. The MAbs were characterized by Western immunoblotting assay and competitive ELISA. The 6 MAbs identify a single neutralization site on a 29K envelope glycoprotein. Deglycosylation of viral proteins prior to immunoblotting showed that the 29K protein is the glycosylated form of a 20K protein. Equine anti-EAV serum also strongly bound the 29K glycoprotein, as well as an unglycosylated protein of 17K. The equine antisera to EAV blocked the binding of a selected MAb to EAV, whereas normal equine serum did not. Two neutralization-resistant escape mutant (EM) variants of the EAV prototype were produced using MAb 6D10. The phenotypic properties of the EM viruses were characterized by neutralization and immunoblotting assays with two

MAbs (6D10 and **5G11**). The two MAbs failed to neutralize either EM virus, and they did not react in an immunoblot assay with any proteins of the EM viruses. In contrast, binding of the equine antiserum to viral proteins was equiv. with prototype and EM virus strains. Thus, a 29K envelope glycoprotein expresses at least one neutralization determinant of EAV.

CC 15-2 (Immunochemistry)

IT Glycoproteins, specific or class
(E (envelope), 29,000-mol.-wt., neutralization epitope on, of equine arteritis virus, **monoclonal** antibody recognition of)

IT Virus, animal
(equine arteritis, envelope glycoprotein of, neutralization epitope on, **monoclonal** antibody recognition of)

IT Antibodies
(**monoclonal**, equine arteritis virus envelope glycoprotein neutralization epitope recognition by)

L18 ANSWER 3 OF 7 HCA COPYRIGHT 1995 ACS

AN 114:22171 HCA

TI Cross-reactive murine **monoclonal** antibodies directed against the core/lipid A region of endotoxin inhibit production of tumor necrosis factor

AU Mayoral, Jaime L.; Dunn, David L.

CS Dep. Surg., Univ. Minnesota, Minneapolis, MN, 55455, USA

SO J. Surg. Res. (1990), 49(4), 287-92
CODEN: JSGRA2; ISSN: 0022-4804

DT Journal

LA English

AB Two murine monoclonal antibodies (mAbs) directed against the core/lipid A moiety of lipopolysaccharide (endotoxin, LPS) were derived from mice immunized with either Escherichia coli J5 or Salmonella minnesota Ra, Rb, Rc, or Re heat-killed organisms or LPS. These mAbs were selected on the basis of their ability to cross-react against a panel of gram-neg. bacterial LPS using Western immunotransblot anal. It was hypothesized that these anti-LPS mAbs directed against the conserved core region of LPS would inhibit LPS-induced macrophage tumor necrosis factor (TNF) prodn. by neutralizing LPS derived from different gram-neg. bacteria. To test this hypothesis, unelicited peritoneal macrophages were treated with either mAb **5G11** (deep core/lipid A specificity, broad LPS cross-reactivity) or mAb 5B11 (intermediate core specificity, limited LPS cross-reactivity). Macrophages were then challenged with a panel of LPS, and TNF activity was measured by the use of the L929 cytotoxicity assay. MAb **5G11** inhibited TNF prodn. against a panel of different types of LPS, but mAb 5B11 did not. In addn., mAb **5G11** did not inhibit TNF prodn. due to isolated lipid A stimulation, suggesting that mAb **5G11** neutralized LPS by binding primarily to the deep core region of LPS. MAb

5G11 was also inhibited TNF prodn. if added within 10 min of LPS stimulation but had no effect at 30 min, suggesting that macrophage stimulation may be irreversible during even the early stages of the response to LPS. Thus, cross-reactive epitopes within the deep core/lipid A region of LPS are highly assocd. with the biol. mediated effects of LPS and a rationale is provided for the clin. use of anti-LPS mAbs which may inhibit the deleterious host mediator-induced effects of endotoxemia.

CC 15-5 (Immunochemistry)

IT Macrophage
(tumor necrosis factor formation by activated, lipopolysaccharide cross-reactive **monoclonal** antibody inhibition of, endotoxemia in relation to)

IT Sepsis and Septicemia
(endotoxemia, lipopolysaccharide cross-reactive **monoclonal** antibodies inhibition of tumor necrosis factor formation by activated macrophage in relation to)

IT Bacteria
(gram-neg., lipopolysaccharides of, **monoclonal** antibodies cross-reactive to, tumor necrosis factor formation by activated macrophage inhibition by, endotoxemia in relation to)

IT Lipopolysaccharides
(lipid A-contg., of gram-neg. bacteria, cross-reactive **monoclonal** antibodies to, tumor necrosis factor formation by macrophage inhibition by, endotoxemia in relation to)

IT Lymphokines and Cytokines
(tumor necrosis factor, formation of, by macrophage, lipopolysaccharide cross-reactive **monoclonal** antibody inhibition of, endotoxemia in relation to)

L18 ANSWER 4 OF 7 HCA COPYRIGHT 1995 ACS

AN 110:132699 HCA

TI Identification of platelet membrane thrombospondin binding molecules using an anti-thrombospondin antibody

AU Kieffer, Nelly; Nurden, Alan T.; Hasitz, Maria; Titeux, Monique; Breton-Gorius, Janine

CS Hop. Henri Mondor, Creteil, Fr.

SO Biochim. Biophys. Acta (1988), 967(3), 408-15
CODEN: BBACAQ; ISSN: 0006-3002

DT Journal

LA English

AB A rat monoclonal IgG2a antibody, **5G11**, was raised against native human platelet thrombospondin (TSP). Western blot anal. revealed that **5G11** bound to TSP before and after SS redn. and to a 15-kDa fragment released after prolonged trypsin digestion. Crossed immunoelectrophoresis confirmed that the binding epitope was expressed in the presence of Ca2+ and after treatment of TSP with EDTA. Since **5G11** had no effect on platelet aggregation, the antibody was used to immunoppt. Ca2+-dependent and

Ca2+-independent TSP-binding mols. on the surface of thrombin-activated 125I surface-labeled platelets. The exptl. basis was that ligand-receptor interactions are of high affinity and that anti-ligand antibodies should ppt. the ligand-receptor complex. With platelets activated in the presence of EDTA, **5G11** predominantly pptd. a 125I-labeled band of Mr 88,000, identified as glycoprotein (GP) IV. In contrast, in the presence of 2 mM Ca2+ and 1 mM Mg2+, **5G11** pptd. a complex of 5 radiolabeled proteins, among which GPIIb, GPIIIa, and BPIV were the most prominent.

CC 13-5 (Mammalian Biochemistry)
Section cross-reference(s): 9

IT Immunoglobulins
(G2a, **monoclonal**, to thrombospondin of human blood platelet)

L18 ANSWER 5 OF 7 HCA COPYRIGHT 1995 ACS
AN 109:188430 HCA
TI Protective **monoclonal** antibodies recognize heat-labile epitopes on surface proteins of spotted fever group rickettsiae
AU Lenz, H. L. B.; Walker, D. H.
CS Med. Branch, Univ. Texas, Galveston, TX, 77550, USA
SO Infect. Immun. (1988), 56(10), 2587-93
CODEN: INFIBR; ISSN: 0019-9567
DT Journal
LA English
AB Thirty-eight monoclonal antibodies (MAbs) were developed from mice immunized with Rickettsia rickettsii, R. conorii, and R. sibirica. Western immunoblotting showed that these MAbs are directed against heat-sensitive epitopes which are located on two major surface polypeptides with mol. sizes ranging from 115 to 150 kilodaltons. Both bands were destroyed by treatment with proteinase K. MAbs examd. by immunofluorescence assay reacted with epitopes that are species-specific, group-reactive, or shared among a smaller subset of species of spotted fever group rickettsiae. Treatment of rickettsiae with MAbs F3-12, F3-14, and F3-36 completely protected guinea pigs against illness caused by the homologous organism R. rickettsii. MAbs F9-**5G11** and F15-5B12, derived from mice immunized with R. sibirica, conferred partial protection by delaying the onset and shortening the duration of fever in guinea pigs inoculated with R. sibirica. MAbs F2-15, F2-31, F2-53, and F3-12 protected mice from a lethal infection with R. conorii. Heat-labile epitopes of spotted fever group rickettsial surface proteins are important candidate antigens for development of vaccines to confer protective immunity.
CC 15-3 (Immunochemistry)
ST **monoclonal** antibody protein spotted fever Rickettsia
IT Antigens
Proteins, biological studies

(heat-labile epitopes of, of spotted fever group rickettsiae, protective **monoclonal** antibodies recognition of)
IT Fever and Hyperthermia
(protection from, by **monoclonal** antibodies to heat-labile proteins of spotted fever group rickettsiae)
IT Rickettsia
(spotted fever group, heat-labile proteins of, protective **monoclonal** antibodies recognition of)
IT Antibodies
(**monoclonal**, heat-labile proteins of spotted fever group rickettsiae recognition by)

L18 ANSWER 6 OF 7 HCA COPYRIGHT 1995 ACS
AN 109:165421 HCA
TI Production and characterization of **monoclonal** antibodies to the macrocyclic trichothecene roridin A
AU Hack, Rudiger; Maertlbauer, Erwin; Terplan, Gerhard
CS Vet. Fac., Univ. Munich, Munich, 8000/22, Fed. Rep. Ger.
SO Appl. Environ. Microbiol. (1988), 54(9), 2328-30
CODEN: AEMIDF; ISSN: 0099-2240
DT Journal
LA English
AB Two murine monoclonal antibodies to the macrocyclic trichothecene roridin A are described. Screening for antibody prodn. was performed on absorbed anti-mouse Ig serum as double-antibody solid phase, and further characterization was done on affinity-purified anti-mouse IgG serum. The antibodies, designated **5G11** and 4H10, had affinity consts. for roridin A of 9.25 .times. 107 and 1.7 .times. 107 L/mol, resp. In monoclonal antibody-based direct enzyme immunoassays, these IgG1 antibodies had detection limits for roridin A of 0.4 ng/mL (0.02 ng per assay) and 1.8 ng/mL (0.09 ng per assay), resp. Both antibodies were most specific for the tested macrocyclic trichothecenes. The relative cross-reactivities of antibody **5G11** with roridin A, roridin J, verrucarin A, satratoxin G, and satratoxin H were 100.0, 43.8, 16.7, 3.7, and 18.9%, resp.; for antibody 4H10 they were 100.0, 6.3, 64.0. 4.4, and 4.9%, resp.
CC 4-5 (Toxicology)
Section cross-reference(s): 15
ST **monoclonal** antibody roridin A
IT Antibodies
(**monoclonal**, to roridin A, prepn. and characterization of)
IT 2198-92-7, Verrucarol 2198-94-9 2270-40-8, Diacetoxyscirpenol 2623-22-5, 15-Acetoxyscirpenol 3148-09-2, Verrucarin A 53126-63-9, Satratoxin G 53126-64-0 74072-83-6, Roridin J
(anti-roridin A **monoclonal** antibodies cross-reactivity with)
IT 14729-29-4, Roridin A

(**monoclonal** antibodies to, prepn. and characterization of)

L18 ANSWER 7 OF 7 HCA COPYRIGHT 1995 ACS
AN 108:71595 HCA
TI Use of a **monoclonal** antibody to measure the surface expression of thrombospondin following platelet activation
AU Legrand, Chantal; Dubernard, Veronique; Kieffer, Nelly; Nurden, Alan T.
CS Hop. Lariboisiere, Paris, F-75010, Fr.
SO Eur. J. Biochem. (1988), 171(1/2), 393-9
CODEN: EJBCAI; ISSN: 0014-2956
DT Journal
LA English
AB The radiolabeled monoclonal antibody **5G11**, directed against native thrombospondin, was used to assess the surface expression of secreted thrombospondin on human blood platelets. Emphasis was placed on studying the role of fibrinogen in this process. Unstimulated platelets bound low amts. of **5G11** (.apprx.2000 mols./platelet). Binding increased 2-fold and 5-7-fold after stimulation of platelets with ADP or thrombin (or ionophore A23187), resp. Unstimulated platelets from patients deficient in .alpha.-granule proteins (gray platelet syndrome) bound baseline levels of **5G11**. However, binding was not increased after activation. Thrombospondin expression on thrombin-stimulated normal platelets was for a large part divalent cation-dependent and was not affected by AP-2, a monoclonal antibody to GPIIb-IIIa complexes. However, binding of **5G11** was some 50% lower when platelets were stimulated in the presence of Fab fragments of a polyclonal rabbit antibody to fibrinogen. This suggested either a direct binding of thrombospondin to surface-bound fibrinogen or a steric inhibition due to a close proximity of the two proteins. The fact that binding of **5G11** was at the lower limit of the normal range to the stimulated platelets of an afibrinogenemic patient specifically lacking detectable fibrinogen favored the latter explanation. Thus, a major fibrinogen-independent pathway for thrombospondin expression must exist.
CC 9-10 (Biochemical Methods)
ST platelet thrombospondin surface expression detn; **monoclonal** antibody thrombospondin platelet; fibrinogen platelet surface thrombospondin
IT Blood platelet
(thrombospondin expression on surface of activating human, fibrinogen role in, **monoclonal** antibody for study of)
IT Fibrinogens
(thrombospondin surface expression on activated human blood platelets response to, **monoclonal** antibodies for study of)
IT Glycoproteins, specific or class

(thrombospondins, surface expression of, on stimulated human blood platelets, fibrinogen role in, **monoclonal** antibody for study of)

=> d bib abs hitind l21 1

L21 ANSWER 1 OF 1 HCA COPYRIGHT 1995 ACS
AN 119:201622 HCA
TI Human immunodeficiency virus type 1 gp120 C5 region mimics the HLA class I .alpha.1 peptide-binding domain
AU Lopalco, Lucia; De Santis, Claudio; Meneveri, Raffaella; Longhi, Renato; Ginelli, Enrico; Grassi, Fabio; Siccardi, Antonio G.; Beretta, Alberto
CS Dip. Ric. Biol. Tecnol., Osp. San Raffaele, Milan, I-20132, Italy
SO Eur. J. Immunol. (1993), 23(8), 2016-21
CODEN: EJIMAF; ISSN: 0014-2980
DT Journal
LA English
AB Mol. mimicry of major histocompatibility (MHC) antigens by viral glycoproteins has been suggested as one of the possible mechanisms of induction of an autoimmune response by human immunodeficiency viruses. A monoclonal antibody (M38) was previously shown to bind to both human immunodeficiency virus type 1 (HIV-1) gp120 and .beta.2-microglobulin-free HLA class I heavy chains encoded by an HLA C allele. Using HLA C recombinant proteins and synthetic peptides, the M38 class I binding site was mapped to a stretch of 44 amino acids of the .alpha.1 domain. The amino acid residues recognized are clustered in two non-contiguous regions at positions 66-69 (KYKR) and 79-82 (RKLR) shared by almost all HLA C alleles. On HIV-1 gp120, M38 binds to two non-contiguous sequences (KYK and KAKR) at positions 490-492 and 505-508 located at the edges of a large hydrophobic region that is apparently involved in binding the transmembrane glycoprotein gp41. The C-terminal gp120 M38-reactive region (KAKR) lies within the immunodominant sequence APTKAKRRVVQREKR, against which the majority of HIV-infected individuals produce antibodies. The results indicate that a functionally important region of HIV-1 gp120 shares similar amino acid sequence motifs with the antigen recognition site of most HLA class I C alleles. The mol. mimicry may be the basis for autoimmune responses in HIV infection.
CC 15-8 (Immunochemistry)
IT Histocompatibility antigens
(HLA-C, **.alpha.**1-**chain** of, **antibody** to HIV-1 virus gp120 **C5** region crossreacting with, epitopes for, mol. mimicry and infection-assocd. autoimmune disease in relation to)
IT Molecular structure-biological activity relationship
(antigenic, of HLA-C antigen **.alpha.**1-**chain** and HIV-1 virus gp120 **C5** region, mol. mimicry in

relation to)
IT **Antibodies**
(crossreacting, to HLA-C **.alpha.**1-**chain** and HIV-1 virus gp120 **C5** region, epitopes for, mol. mimicry and infection-assocd. autoimmune disease in relation to)
IT Sialoglycoproteins
(gp120env, **C5** region of, of HIV-1 virus, **antibody** to HLA-C antigen **.alpha.**1-**chain** crossreacting with, epitopes for, mol. mimicry and infection-assocd. autoimmune disease in relation to)
IT Virus, animal
(human immunodeficiency 1, gp120 glycoprotein of, **C5** region of, **antibody** to HLA-C antigen **.alpha.**1-**chain** crossreacting with, epitopes for, mol. mimicry and infection-assocd. autoimmune disease in relation to)

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	DEL	HIS	Y
L1	0	S	5G1 1 OR 5 G1 1
L2	2	S	5G1
L3	0	S	5G46K OR 5G27K OR 5G200AA OR KSSKC
L4	1	S	5G 46K OR 5G 27K OR 5G 200## OR KSSKC
L5	0	S	C5G46K OR C5G27K OR C5G200AA OR KSSKC
L6	0	S	C5G 46K OR C5G 27K OR C5G 200## OR KSSKC
L7	3971	S	C5
L8	21384	S	NEPHRITIS OR GLOMERULONEPH?
L9	70	S	L7 AND L8
L10	23	S	L9 AND ANTIBOD?
L11	8	S	L10 AND MONOCLONAL?
L12	15	S	L10 NOT L11
L13	10329	S	ALPHA (2A) CHAIN#

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L14          78 S L7 AND L13
L15          15 S L14 AND ANTIBOD?
L16          15 S L15 NOT (L12 OR L11)
L17           2 S COMPLEMENT C 5
L18           6 S COMPLEMENT AND C 5
L19           0 S L18 AND L8
L20          74 S C5A (L) CLEAVAGE#
L21           1 S C5A (L) CLEAVAGE SITE
L22           1 S C5A AND CLEAVAGE SITE#
L23           1 S L21 OR L22

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L11  ANSWER 1 OF 8  BIOSIS  COPYRIGHT 1995 BIOSIS
AN  93:462025  BIOSIS
DN  BA96:106925
TI  ACTIVATED C3 C3B IN THE NEPHRITIC GLOMERULUS.
AU  PAN C; STRIFE C F; MCADAMS A J; WEST C D
CS  DIV. NEPHROLOGY, CHILDREN'S HOSP. RES. FOUNDATION, CINCINNATI, OH
    45229, USA.
SO  PEDIATR NEPHROL 7 (4). 1993.  379-386. CODEN: PEDNEF
LA  English
AB  An autoradiographic technique was developed to assess in the
    nephritic glomerulus the relative amount of C3 which is in the
    activated form, C3b, compared with the inactivated form, iC3b. Frozen
    renal biopsy sections from children and young adults with
    glomerulonephritis were assessed for the C3b fraction of
    total C3, using a radiolabeled monoclonal anti-C3c. Grain
    counts with this antibody, before and after reacting the
    section with 0.0002% trypsin, gave the relative amounts of total C3
    and  C3b, respectively. C3b was found in all diseases studied. To
    explain its presence, glomerular C3b acceptors which would restrict
    C3b inactivation were sought by immunofluorescence studies. C3b
    acceptor candidates were: IgG in aggregated form, IgA as found in the
    IgA nephropathies and the C3/C5 convertase, C4b,2a,3b. In
    acute post-streptococcal glomerulonephritis and
    membranoproliferative glomerulonephritis type III, diseases
    in which these acceptors were lacking, it is postulated that the
    nephritis strain-associated protein and absence of membrane
    cofactor protein, respectively, may be responsible for C3b
    deposition. The phlogistic effect of C3b is mediated largely by one
    of its products, C5b-9. However, the C3b: total C3 ratio failed to
    correlate with indices of glomerular inflammation, probably in part
    because the ratio is not a measure of total glomerular C3b.

L11  ANSWER 2 OF 8  BIOSIS  COPYRIGHT 1995 BIOSIS
AN  91:461919  BIOSIS
DN  BA92:106699
TI  URINARY EXCRETION OF TERMINAL COMPLEMENT COMPLEXES IN GLOMERULAR
```

DISEASE.
AU KUSUNOKI Y; AKUTSU Y; ITAMI N; TOCHIMARU H; NAGATA Y; TAKEKOSHI Y; SAGAWA A; KATAOKA Y; NAGASAWA S
CS VARIETY CLUB CHILDREN'S HOSP. PEDIATRIC NEPHROLOGY, BOX 491, UMHC, 515 DELAWARE STREET SE, MINNEAPOLIS, MINN. 55455, USA.
SO NEPHRON 59 (1). 1991. 27-32. CODEN: NPRNAY ISSN: 0028-2766
LA English
AB To evaluate renal terminal complement activation in patients with glomerular diseases, we measured terminal complement complexes (TCCs) in plasma and urine with sandwich enzyme-linked immunosorbent assay (ELISA) using a **monoclonal antibody** against a C9 neoepitope expressed on TCC and a polyclonal antihuman C7 **antibody**. TCCs were detectable in plasma but not in urine in most of normal controls. In plasma, TCC levels were elevated in 4 of 22 patients with lupus **nephritis** and in 6 of 12 with membranoproliferative **glomerulonephritis**. However all patients with IgA **nephritis**, focal glomerulosclerosis, idiopathic membranous **nephritis** and idiopathic minimal change nephrotic syndrome (MC) showed normal values. In urine, TCCs were detectable in almost all patients with heavy proteinuria (.gtoreq. 100 mg/ml) except MC. The TCCs present in urine were partially purified by gel filtration using Sepharose 6B and were found to contain **C5**, C6, C7, C8, C9 and S protein by ELISA. Although the molecular weight of TCC is similar to that of IgM, the fractional excretion rate of TCC was about 100 times higher than that of IgM. These results suggest that TCCs detectable in urine contain SC5b-9 complexes and are mostly of renal origin.

L11 ANSWER 3 OF 8 BIOSIS COPYRIGHT 1995 BIOSIS
AN 91:27235 BIOSIS
DN BA91:16586
TI A RAT HYBRIDOMA MODEL OF HEYMANN **NEPHRITIS** PRODUCTION OF A **MONOCLONAL** ANTI-GP330 FROM A NEPHRITIC RAT.
AU BEHAR M; KATZ A; SILVERMAN M
CS MED. SCI. BUILD., ROOM 7226, 8 TADDLE CREEK ROAD, UNIV. TORONTO, TORONTO, ONTARIO M5S 1A8.
SO CLIN INVEST MED 13 (5). 1990. 264-270. CODEN: CNVMDL ISSN: 0147-958X
LA English
AB Autologous (Heymann) **nephritis** was induced by immunizing Sprague-Dawley rats with a crude membrane extract (Fx1A) prepared from renal cortical tubules. Urine protein excretion was monitored to determine the onset of **nephritis** and then the spleens of nephritic rats were fused with a non-secretor rat myeloma cell line. Supernatants from hybridoma cultures were first screened for production of anti-brush border membrane (BBM) **antibody** by immunodot blotting of highly purified rat BBM on nitrocellulose. Positive hybrids were then tested by indirect immunofluorescence for the presence of IgG, which binds to the brush border of rat renal proximal tubules. Those hybrids which were positive by both screening

assays were subcloned twice. Two **monoclonal antibodies** (**C5**, D11) were studied in some detail. Both **C5** and D11 immunoprecipitated a single polypeptide from BBM, labelled with 125I by the lactoperoxidase method. Radioautography of gradient 4-11% slab sodium dodecyl sulphate polyacrylamide gels revealed that the polypeptide against which **C5** and D11 were directed co-migrated with the polypeptide immunoprecipitated by (i) IgG eluted from the renal cortex of nephritic rats, and by (ii) a mouse anti-rat **monoclonal** against gp 330 [a BBM constituent with proven pathogenicity [9]]. Supernatants which tested positive by immunodot blotting but negative by indirect immunofluorescence showed no detectable immunoprecipitate after reaction with BBM. Immunocytochemical staining by immunoperoxidase and immunogold methods localized **C5** and D11 to the BBM of the renal proximal tubule and to the urine face of the glomerular epithelium. Competition experiments of Western blot show that anti-gp 330 **monoclonal antibody** and our rat **monoclonal antibody C5** compete for the same antigen in the rat BBM, thus confirming that **C5** is directed against gp 330. These results confirm by a novel approach the important role of gp 330 as a specific immunogen in active Heymann **nephritis**. This rat hybridoma model should now permit a more detailed assessment of other anti-kidney **antibodies** that could play a role in Heymann **nephritis** pathogenicity.

L11 ANSWER 4 OF 8 BIOSIS COPYRIGHT 1995 BIOSIS
AN 90:332246 BIOSIS
DN BA90:40265
TI MEMBRANE ATTACK COMPLEX OF COMPLEMENT IN HENOCH-SCHOENLEIN PURPURA SKIN AND **NEPHRITIS**.
AU KAWANA S; SHEN G H; KOBAYASHI Y; NISHIYAMA S
CS DEP. DERMATOL., KITASATO UNIV. SCH. MED., 1-15-1 KITASATO, SAGAMIHARA, KANAGAWA 228, JPN.
SO ARCH DERMATOL RES 282 (3). 1990. 183-187. CODEN: ADREDL ISSN: 0340-3696
LA English
AB The present study using direct immunofluorescence with **monoclonal antibodies** to C5b-9 complex-related antigens was undertaken to determine whether complement activation in Henoch-Schonlein purpura (HSP) causes assembly of the membrane attack complex of complement (MAC) in skin and **nephritis** lesions. The deposition of **C5**, C6, C7, C8, C9, and C5b-9 neoantigens was noted in the vascular walls of papillary dermis and/or subpapillary dermal plexus of the vessels in 11 out of 15 patients with HSP. Their presence in vessel walls indicates complement activation which leads to terminal complement activation. There were small deposits of S protein at the same sites in three of the 11 skin specimens. Thus, the majority of C5b-9 demonstrated in HSP skin was

the cytolytically active C5b-9 complex, MAC. Granular deposits of C5b-9 related antigens without S protein were also found in the capillary walls and mesangium of the glomeruli of two out of four specimens from patients with HSP **nephritis**; in the other two S protein was colocalized with the deposition of C5b-9. The results of the present study indicate that complement activation leading to generation of MAC may possibly be involved in the pathogenesis of vascular injury in a significantly large number of skin lesions and of HSP **nephritis**.

L11 ANSWER 5 OF 8 BIOSIS COPYRIGHT 1995 BIOSIS
AN 90:262243 BIOSIS
DN BA90:4329
TI TERMINAL COMPLEMENT COMPLEX TCC LEVELS IN PLASMA AND URINE FROM GLOMERULAR DISEASES ENZYME-LINKED IMMUNOSORBENT ASSAY ELISA USING **MONOCLONAL ANTIBODY** AGAINST NEOANTIGENS OF TCC.
AU KUSUNOKI Y
CS DEP. PEDIATR., HOKKAIDO UNIV. SCH. MED., SAPPORO 060, JPN.
SO HOKKAIDO J MED SCI 65 (1). 1990. 74-85. CODEN: HOIZAK ISSN: 0367-6102
LA Japanese
AB In order to get **monoclonal antibodies** (MoAbs) against neoantigens of terminal complement complex, MoAbs after immunization of mice with polymerized human C9 were screened for reactivities against native and polymerized C9. MoAb 1B4 reacted with tubular C9 polymer, but did not react with either native or sodium dodecyl sulfate-denatured monomeric C9 as revealed by enzyme-linked immunosorbent assay (ELISA) and Western blotting. Moreover, MoAb 1B4 reacted with the terminal complement complex (TCC) that is, membrane attack complex the fluid-phase SC5b-9 complex. Thus, MoAb 1B4 recognized a neoantigen in the moiety of C9 polymer in the TCC. Thereafter, we measured TCC in plasma and urine with sandwich ELISA using 1B4 and antihuman C7 **antibody** to evaluate terminal complement activation in patients with glomerular diseases. TCC was detectable in plasma but not in urine from most of normal controls. In plasma, TCC was evaluated in 5 of 23 with lupus **nephritis** and in 6 of 11 with membranoproliferative **glomerulonephritis** , but all patients with IgA **nephritis**, focal glomerulosclerosis, membranous **glomerulonephritis** and minimal change lesions (MC) showed normal levels. In urine, TCC was detectable in most of patients with severe proteinuria (.gtoreq. 100 mg/dl) except MC. The TCC present in urine was partially purified by gel filtration with Sepharose 6B and was found to contain **C5** , C6, C7, C8, C9, and S protein by ELISA. Although the molecular weight of SC5b-9 complex is similar to IgM, fractional excretion rate of TCC was about 100 times higher than that of IgM. These results suggest that urinary TCC contains SC5b-9 complex like plasma TCC and is mostly derived from renal origin.

L11 ANSWER 6 OF 8 BIOSIS COPYRIGHT 1995 BIOSIS
AN 87:111792 BIOSIS
DN BA83:60770
TI **GLOMERULONEPHRITIS** INDUCED BY **MONOCLONAL** ANTI-THY 1.1 **ANTIBODIES** A SEQUENTIAL HISTOLOGICAL AND ULTRASTRUCTURAL STUDY IN THE RAT.
AU BAGCHUS W M; HOEDEMAEKER P J; ROZING J; BAKKER W W
CS DEP. OF PATHOL., UNIV. OF GRONINGEN, GRONINGEN.
SO LAB INVEST 55 (6). 1986. 680-687. CODEN: LAINAW ISSN: 0023-6837
LA English
AB The present report describes the natural history of an experimental acute **glomerulonephritis** with massive proteinuria induced by a single intravenous injection of a (mouse) **monoclonal** anti-rat Thy 1.1 **antibody** into the rat. The disease is characterized by direct although transient binding of this **monoclonal antibody** to glomerular basement membrane and mesangium after injection as demonstrated by immunofluorescence microscopy. Immediate activation of complement occurs as shown by glomerular deposition of C3 and C9. Concomitant activation of the coagulation cascade is reflected by the presence of fibrinogen deposits in the affected glomeruli. One hour after injection mesangial alterations are prominent including condensation of mesangial cell chromatin, and lysis of mesangial cells as shown by light- and electron-microscopy, leading to the formation of aneurysms in the capillary tuft. Commencing on day 4 mesangial cell proliferation can be observed, accompanied by glomerular crescent formation at day 14, which decreases gradually 3 weeks after **antibody** administration, whereas mesangial hypercellularity can be observed up to week 10 after intravenous injection of the **antibody**. The disease is clinically characterized by a massive transient proteinuria starting immediately after **antibody** injection, reaching mean values of 300 mg/24 hours at days 2 to 4, gradually decreasing to normal levels after 3 weeks. It is concluded that in this unique model of **glomerulonephritis** induced by a **monoclonal antibody**, recognition of Thy 1.1 epitopes as well as activation of complement including the **C5**-C9 membrane attack complex may play a major role in the pathogenesis of this experimental disease.

L11 ANSWER 7 OF 8 BIOSIS COPYRIGHT 1995 BIOSIS
AN 85:278838 BIOSIS
DN BA79:58834
TI CELL POPULATIONS AND MEMBRANE ATTACK COMPLEX IN GLOMERULI OF PATIENTS WITH POST-STREPTOCOCCAL **GLOMERULONEPHRITIS** IDENTIFICATION USING **MONOCLONAL ANTIBODIES** BY INDIRECT IMMUNOFLUORESCENCE.
AU PARRA G; PLATT J L; FALK R J; RODRIGUEZ-ITURBE B; MICHAEL A F
CS DEP. PEDIATR., UNIV. MINN. MED. SCH., MINNEAPOLIS, MINN. 55455, USA.

SO CLIN IMMUNOL IMMUNOPATHOL 33 (3). 1984. 324-332. CODEN: CLIIAT ISSN: 0090-1229
LA English
AB Poststreptococcal **glomerulonephritis** (PSGN) had been thought to arise from renal deposition of immune complexes and as such is analogous to acute serum sickness. Recent studies of acute serum sickness in animals and PSGN in humans, however, have suggested a pathogenetic role for cellular immunity. To enlarge on these observations, cellular components of glomeruli were characterized by indirect immunofluorescence in 11 tissues from individuals with PSGN using **monoclonal antibodies**. These studies demonstrate infiltration of glomeruli by monocytes, granulocytes and lymphoid cells. Focal accumulations of T lymphocytes were also observed adjacent to Bowman's capsule. Analysis of glomerular T cell subpopulations revealed a predominance of cells reactive with OKT4 early and with OKT8 later in the course of disease. Proliferation of parietal and visceral epithelial cells was associated with increased binding of BA-1 and J5, respectively. The presence of the membrane attack complex of complement was demonstrated by glomerular reactivity with a **monoclonal antibody** (poly-C9 [complement component 9] MA) which recognizes a neoantigen present in poly-C9 [complement component 9]. Fluorescence was present along the glomerular basement membrane early and within the mesangium late in the course of disease, a distribution similar to that observed for C3 and **C5**. The observations suggest that immune cells as well as terminal components of complement either provoke or mark tissue injury in PSGN.

L11 ANSWER 8 OF 8 BIOSIS COPYRIGHT 1995 BIOSIS
AN 84:275145 BIOSIS
DN BA78:11625
TI NEO ANTIGEN OF POLYMERIZED COMPLEMENT C-9 CHARACTERIZATION OF A MONO CLONAL **ANTIBODY** AND IMMUNO HISTOCHEMICAL LOCALIZATION IN RENAL DISEASE.
AU FALK R J; DALMASSO A P; KIM Y; TSAI C H; SCHEINMAN J I; GEWURZ H; MICHAEL A F
CS DEP. PEDIATR., UNIV. MINN. MED. SCH., VETERANS ADM. MED. CENT., MINNEAPOLIS, MINN. 55455.
SO J CLIN INVEST 72 (2). 1983. 560-573. CODEN: JCINAO ISSN: 0021-9738
LA English
AB A **monoclonal antibody** to a neoantigen of the C9 [complement component 9] portion of the membrane attack complex (MAC) of human complement was developed and characterized. The distribution of this neoantigen was assessed by indirect immunofluorescence microscopy in nephritic and nonnephritic renal diseases. The **antibody** (Poly C9-MA) reacted on enzyme-linked immunosorbent assay (ELISA) with a determinant in complement-activated serum that was undetectable in normal human serum (NHS). Zymosan particles incubated in NHS had positive immunofluorescent staining with Poly

C9-MA; binding of Poly C9-MA was not observed with zymosan particles incubated in sera deficient in individual complement components C3, **C5**, C6, C7, C8 or C9. Reconstitution of C9-deficient sera with purified C9 restored the fluorescence with Poly C9-MA. Poly C9-MA reacted positively by ELISA in a dose-dependent manner with purified MC5b-9 solubilized from membranes of **antibody** -coated sheep erythrocytes treated with NHS but not with intermediate complement complexes. Poly C9-MA also reacted in a dose-dependent manner on ELISA and in a radioimmunoassay with polymerized C9 (37.degree. C, 64 h) (poly C9) but not with monomeric C9. Increasing amounts of either unlabeled poly C9 or purified MC5b-9 inhibited the 125I-poly C9 RIA in an identical manner. Evidently, Poly C9-MA recognizes a neoantigen of C9 common to both the MAC and to poly C9. By immunofluorescence, Poly C9-MA reacted minimally with normal kidney tissue in juxtaglomerular loci, the mesangial stalk and vessel walls. Poly C9-MA stained kidney tissue from patients with **glomerulonephritis** in a pattern similar to that seen with polyclonal anti-human C3. In tissue from patients with nonnephritic renal disease, diabetes, hypertension and obstructive uropathy, Poly C9-MA was strongly reactive in the mesangial stalk and juxtaglomerular regions, tubular basement membranes and vascular walls. Poly C9-MA binding was especially prominent in areas of advanced tissue injury. Poly C9-MA frequently stained loci where C3 was either minimally present or absent. These studies provide strong evidence for complement activation not only in nephritic but also in nonnephritic renal diseases.

L12 ANSWER 1 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 94:413831 BIOSIS
DN 97426831
TI C5b-9 increases albumin permeability of isolated glomeruli in vitro.
AU Savin V J; Johnson R J; Couser W G
CS Div. Nephrol., 4015 Sudler, Univ. Kansas Med. Cent., 39th and Rainbow Blvd., Kansas City, KS 66160-7382, USA
SO Kidney International 46 (2). 1994. 382-387. ISSN: 0085-2538
LA English
AB Deposition of **antibody** and activation of the complement cascade are important in both naturally occurring **glomerulonephritis** and in experimental models including passive Heymann **nephritis**. We studied the effect of **antibody** and complement on albumin permeability of isolated glomeruli to determine the role of the terminal complement components (**C5**-C9) in mediating the proteinuria in **nephritis** . Isolated glomeruli were treated with anti-Fx1a (Heymann **antibody**) and then incubated them with pooled human serum, serum in which complement had been inactivated by heat, or serum deficient in C6 or C7. The albumin reflection coefficient

(sigma-albumin) was calculated from the volumetric response of glomeruli to transcapillary oncotic gradients produced by albumin or high molecular weight neutral dextran (252 kD). Convectional permeability to albumin (P-albumin) was calculated as 1-sigma-albumin. Albumin permeability of control glomeruli was not different from 0. Albumin permeability was not altered by **antibody** alone but was increased to 0.65 +- 0.04 when **antibody** treated glomeruli were incubated for 10 minutes with pooled serum as a source of complement. Heat treatment of serum to inactivate complement prevented the increase in permeability. Incubation for 10 minutes with serum without **antibody** pretreatment caused a lesser increase in permeability of isolated glomeruli (0.18 +- 0.06). Serum deficient in either C6 or C7 did not cause an increase in albumin permeability of **antibody** pre-treated glomeruli, but incubation with a combination of these sera (now containing the complete cascade) increased permeability to the same extent as did pooled normal serum (0.58 +- 0.04). We conclude that activation of the terminal complement components is required for the increase in glomerular macromolecular permeability caused by anti-Fxla and that terminal complement activation is sufficient to alter the permeability independent of complement hemodynamic events or contribution by circulating cells.

L12 ANSWER 2 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 92:280586 BIOSIS
DN BA94:5236
TI STUDY OF THE IDIOTYPIC RESPONSE TO AUTOANTIBODY TO THE ALTERNATIVE PATHWAY C3-**C5** CONVERTASE IN NORMAL INDIVIDUALS PATIENTS WITH MEMBRANOPROLIFERATIVE **GLOMERULONEPHRITIS** AND EXPERIMENTAL ANIMALS.
AU SPITZER R E; STITZEL A E; TSOKOS G C
CS DEP. PEDIATR., SUNY HEALTH SCI. CENT. SYRACUSE, SYRACUSE, N.Y. 13210.
SO CLIN IMMUNOL IMMUNOPATHOL 62 (3). 1992. 291-294. CODEN: CLIIAT ISSN: 0090-1229
LA English
AB We studied the fluctuation of autoantibody to the alternative pathway C3/**C5** convertase (C3NeF) and its autoantiidiotypic **antibodies**, Ab2.alpha. and Ab2.beta., in normal individuals, patients with membranoproliferative **glomerulonephritis** (MPGN), and New Zealand white rabbits. In normal individuals, serum levels of Ab2.alpha. (anti-id Ab without internal imagery to the native antigen) are several times higher than those of Ab2.beta. (anti-id Ab bearing the internal image of the native antigen). When normal rabbits are immunized with Ab2.beta., Ab3 is produced which has strong C3NeF activity. Ab3 acts to stimulate the prompt production of Ab4a. Ab3 (C3NeF) titers than fall, followed by the appearance of Ab4.beta.. Patients with MPGN and C3NeF activity were also studied. Untreated patients at the time of diagnosis have a two- to fourfold predominance of Ab2.beta. which is a direct reversal of

the normal situation. When the patients were treated with prednisone. C3NeF levels fell and Ab2.alpha. again predominated. These data suggest that the idiotypic network acts to control the production of autoantibody in a balanced fashion. Moreover, these data suggest that the patients response to Ab1 is quite different than that found in normal individuals.

L12 ANSWER 3 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 92:119440 BIOSIS
DN BA93:65240
TI AUTOANTIBODY TO THE ALTERNATIVE PATHWAY C3-**C5** CONVERTASE AND ITS ANTI-IDIOTYPIC RESPONSE A STUDY IN AFFINITY.
AU SPITZER R E; STITZEL A E; TSOKOS G C
CS DEP. PEDIATRICS, STATE UNIV. NEW YORK HEALTH SCIENCE CENT., 750 EAST AFAMS STREET, SYRACUSE, N.Y. 13210.
SO J IMMUNOL 148 (1). 1992. 137-141. CODEN: JOIMA3 ISSN: 0022-1767
LA English
AB In an effort to understand the development and control of autoantibody production, we studied the affinity of autoantibody to the alternative pathway C3/**C5** convertase (C3 nephritic factor (C3NeF)) and its autoanti-idiotypic **antibodies**, Ab2.alpha. and Ab2.beta.. These were isolated and purified from newborns, normal adults, and patients with membranoproliferative **glomerulonephritis**. In all cases, both IgG and IgM C3NeF were available for study. The affinity of IgG and IgM C3NeF for their natural Ag (108 liters/mol) as well as for the internal image of that Ag displayed on Ab2.beta. was high (1010 liters/mol). Furthermore, the affinity of IgG C3NeF was nearly 100-fold higher in patients than in newborns, whereas there were no significant changes with IgM C3NeF. By contrast, there were no differences in the affinity of IgG Ab2.alpha. (which does not display any likeness to the native Ag) from normal adults and patients to any C3NeF isolate. There was, however, a progressive increase in affinity between both Ab2.alpha. preparations and IgG C3NeF from newborns, adult normal subjects, and patients, implying an alteration in C3NeF to account for the changes in affinity. These data suggest that Ag-driven affinity maturation occurs with autoantibody but may not occur within the idiotypic network. These data also indicate that as autoantibody affinity matures, it appears to modify its idiotype, perhaps in an effort towards autoregulation.

L12 ANSWER 4 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 92:79144 BIOSIS
DN BA93:47599
TI COMPLEMENT ACTIVATION INDUCES THE EXPRESSION OF DECAY-ACCELERATING FACTOR ON HUMAN MESANGIAL CELLS.
AU SHIBATA T; COSIO F G; BIRMINGHAM D J
CS DEP. INTERNAL MED., OHIO STATE UNIV., 1654 UPHAM DR., ROOM N210, COLUMBUS, OHIO 43210-1228.

SO J IMMUNOL 147 (11). 1991. 3901-3908. CODEN: JOIMA3 ISSN: 0022-1767
LA English
AB In the present study we evaluated the effect of complement activation by immune complexes (IC) on the expression of decay-accelerating factor (DAF) on human mesangial cells (MC). MC in culture were incubated with an Ag (DNP-Gelatin) that binds to fibronectin present in the MC matrix. Subsequently, MC were incubated with anti-DNP **antibodies** in the presence of human serum. By immunoperoxidase staining we showed that these incubations resulted in IC formation and deposition of human C3 and terminal complement components (C5b-9) on the mesangial matrix and on the surface of MC. By immunoperoxidase staining and by RIA we showed that IC formation and complement activation significantly increased DAF expression on the MC plasma membrane. The induction of DAF expression was a consequence of deposition of terminal complement components on the MC because, zymosan-activated serum and IC formation in the presence of **C5**- or C8-deficient serum failed to increase MC DAF expression. Furthermore, the observed increased DAF expression was the consequence of increased DAF synthesis by MC. Thus, both cycloheximide and actinomycin D blocked the increase on MC DAF observed after incubation with IC and serum. MC DAF had biophysical and functional characteristics similar to DAF in other cells. Thus, 1) MC DAF was resistant to trypsin but was removed from the MC membrane by pronase; 2) phosphatidylinositol-specific phospholipase C removed 48 .+-. 4% of MC DAF indicating that MC DAF is anchored in the cell membrane by phosphatidylinositol groups; 3) DAF isolated from MC-inhibited complement-mediated hemolysis and demonstrated a molecular mass of 83 kDa. In conclusion, deposition of terminal complement components on human MC trigger new synthesis and membrane expression of DAF. Because DAF protects cells against complement-mediated lysis, we postulate that DAF may protect glomerular cells during IC and complement-mediated **glomerulonephritis**.

L12 ANSWER 5 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 91:485499 BIOSIS
DN BA92:119259
TI ELEVATED URINARY EXCRETION OF THE C5B-9 COMPLEX IN MEMBRANOUS NEPHROPATHY.
AU SCHULZE M; DONADIO J V JR; PRUCHNO C J; BAKER P J; JOHNSON R J; STAHL R A K; WATKINS S; MARTIN D C; WURZNER R; ET AL
CS DIV. NEPHROL., ROOM 11, DEP. MED., UNIV. WASH. SCH. MED., SEATTLE, WASH. 98195.
SO KIDNEY INT 40 (3). 1991. 533-538. CODEN: KDYIA5 ISSN: 0085-2538
LA English
AB In experimental membranous nephropathy, **antibody** binding to glomerular epithelial cell membrane antigens results in complement activation and formation of complement C5b-9 membrane attack complexes in glomeruli. During active disease, the C5b-9 complexes

are shed into the urine. To test the hypothesis that a similar mechanism might be operative in human membranous nephropathy, we measured urinary excretion of C5b-9 and **C5** in 146 proteinuric patients with biopsy-proven glomerular diseases or diabetes mellitus. Urinary excretion of C5b-9 relative to **C5** excretion was higher in 40 patients with membraneous nephropathy than in 106 patients with proteinuria due to non-membranous **glomerulonephritis** when analyzed by covariance analysis ($P < 0.0002$). Urinary C5b-9 excretion was higher in membranous nephropathy than in membranoproliferative **glomerulonephritis** ($N = 13$, $P < 0.05$), minimal change-focal sclerosis ($N = 33$, $P < 0.001$), mesangial proliferative **glomerulonephritis** ($N = 9$, $P < 0.02$) and IgA nephropathy ($N = 7$, $P < 0.025$). Urinary C5b-9 excretion was also higher in patients with lupus **nephritis** ($N = 18$, $P < 0.02$) compared to those with non-membranous **glomerulonephritis**. The lupus patients with the highest excretion had clinical or pathological features of membranous nephropathy. Nine patients with membranous nephropathy and elevated urinary C5b-9 excretion had a shorter duration of disease ($P < 0.05$), lower serum creatinine levels ($P < 0.05$) and more proteinuria ($P < 0.02$) than the 31 membranous nephropathy patients with normal values. The finding of increased urinary C5B-9 excretion in a subset of patients with idiopathic or lupus membranous nephropathy suggests an autoimmune basis for glomerular disease in these patients, and may indicate that these patients have ongoing immune deposit formation.

L16 ANSWER 1 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 94:547913 BIOSIS
DN 98007461
TI Recombinant expression and properties of the Kunitz-type protease-inhibitor module from human type VI collagen **alpha** -3(VI) **chain**.
AU Mayer U; Poeschl E; Nischt R; Specks U; Pan T-C; Chu M-L; Timpl R
CS Max-Planck-Inst. Biochem., D-82152 Martinsried, Germany
SO European Journal of Biochemistry 225 (2). 1994. 573-580. ISSN: 0014-2956
LA English
AB The Kunitz-type inhibitor motif (domain **C5**) present at the C-terminus of the human collagen **alpha**-3(VI) **chain** was prepared in a recombinant form from the culture medium of stably transfected kidney cell clones. The 76-residue protein was disulfide bonded and showed a high stability against protease treatment. The recombinant protein lacked, however. any inhibitory activity for trypsin, thrombin, kallikrein and several other proteases, which could be due to a few unusual substitutions in the region crucial for inhibitor binding. A sensitive radioimmunoassay detected low concentrations of **C5** epitopes in normal human serum and

fibroblast culture medium and showed a lack of cross-reaction with aprotinin. **Antibodies** against **C5** immunoprecipitated collagen VI obtained from fibroblast medium. The **C5** epitopes could not be detected on intact collagen VI purified from guanidine extracts of human placenta. Collagen VI was shown to possess several **alpha**-3(VI) **chain** bands (approximately 200 kDa) and reacted strongly with **antibodies** to an N-terminal recombinant fragment. Immunofluorescence with anti-**C5 antibodies** failed to stain several human tissues but produced a distinct intracellular staining of cultured fibroblasts. The data indicate the rapid loss of the **C5** domain after biosynthesis of collagen VI.

L16 ANSWER 2 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 94:251764 BIOSIS
DN 97264764
TI Signal transduction via Fc-gamma-R and Mac-1 **alpha-chain** in monocytes and polymorphonuclear leucocytes.
AU Gadd S J; Eher R; Majdic O; Knapp W
CS Inst. Immunol., University Vienna, Borschkegasse 8a, A-1090, Vienna, AUS
SO Immunology 81 (4). 1994. 611-617. ISSN: 0019-2805
LA English
AB Some (VIM12, Leu-15,5A4.**C5**), but not all, Mac-1-specific monoclonal **antibodies** (mAb) induced a clear respiratory burst in unprimed monocytes but not in unprimed polymorphonuclear leucocytes (PMN). We showed that this monocyte stimulation occurred via formation of Mac-1 mAb-Fc-gamma-RI or Mac-1 mAb-Fc-gamma-RII complexes, as human monomeric IgG1 could completely block the respiratory burst induced by the murine IgG2a subclass anti-Mac-1 mAb Leu-15 and the Fc-gamma-RII-specific mAb IV.3 inhibited respiratory burst formation by IgG1) subclass anti-Mac-1 mAb VIM12 and 5A4. **C5**, respectively. F(ab')-2 fragments of mAb VIM12 did not stimulate. This association between Mac-1 and Fc-gamma-RII may be due to a near spatial association between these molecules in monocytes, as we observed partial inhibition of FITC-labelled anti-Fc-gamma-RII mAb IV.3 binding after prior incubation with mAb VIM12. If monocytes were preincubated with mAb IV.3 or aggregated IgG, there was partial inhibition of mAb VIM12 binding. The non-stimulating anti-Mac-1 mAb (JML.H11,44, OKM1, LM2/1, Mol) did not show any significant competition with mAb IV.3 binding to Fc-gamma-RII. Both non-stimulating CD18-specific mAb, however, showed strong competition with mAb IV.3 binding to Fc-gamma-RII. On unprimed PMN, the situation was different. No Mac-1-specific mAb induced a respiratory burst and there was no competitive inhibition between anti-Mac-1 mAb and **antibodies** binding to Fc-gamma-RII. In interferon-gamma (IFN-gamma)-primed PMN, however, we observed a functional association between Mac-1 and Fc-gamma-RI as IgG2a subclass mAb Leu-15 induced a respiratory burst which could be inhibited by monomeric human IgG1,

as observed in monocytes. However, no other anti-Mac-1 mAb was able to induce a respiratory burst in IFN-gamma-primed PMN. Therefore, a similar signal transducing capability may exist between Mac-1 and Fc-gamma-RI on both monocytes and PMN, despite a different relationship between Mac-1 and Fc-gamma-RII on these cell populations. As no Mac-1 beta-chain-specific (CD18) mAb were able to induce a respiratory burst in monocytes, despite being able Fc-gamma-RII, we conclude that intracellular signalling via Mac-1 mAb-Fc-gamma-RII complexes requires the **alpha-chain**
.

L16 ANSWER 3 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 93:143342 BIOSIS
DN BA95:76142
TI MOLECULAR BASIS OF COMPLEMENT RESISTANCE OF HUMAN MELANOMA CELLS EXPRESSING THE C3-CLEAVING MEMBRANE PROTEASE P65.
AU OLLERT M W; KADLEC J V; PETRELLA E C; BREDEHORST R; VOGEL C-W
CS DEP. BIOCHEM. MOLECULAR BIOL., UNIV. HAMBURG, MARTIN-LUTHER-KING-PL. 6, 2000 HAMBURG 13, GER.
SO CANCER RES 53 (3). 1993. 592-599. CODEN: CNREA8 ISSN: 0008-5472
LA English
AB The molecular mechanism of complement resistance of the human SK-MEL-170 melanoma cell line was investigated. The cells have been shown to express the C3b-cleaving membrane protease p65. To delineate the molecular consequences of the C3b-cleaving activity for the complement cytotoxicity, the molecular events during the initiation (R24 monoclonal **antibody**, C1), amplification (C4, C3), and membrane attack (**C5**, C9) phases of complement were studied in comparison to a complement-susceptible human melanoma line (SK-MEL-93-2). No cleavage of C4b and C5b, 2 molecules structurally similar to C3b, was observed on the cells during classical pathway activation indicating the specificity of the p65 protease for the C3b molecule. The rapid degradation of C3b by p65 on the surface of complement-resistant SK-MEL-170 cells generates a Mr 30,000 C3. **alpha**.'-**chain**-fragment detectable as early as 1 min after complement activation, whereas no such fragment was present in detectable amounts on complement-susceptible cells. As a result of the rapid C3b proteolysis by p65 on resistant SK-MEL-170 cells, less **C5** convertases are formed, which in turn results in the formation of a lower number of terminal complement components and membrane attack complexes. R24 **antibody** and C1q binding to the resistant cells was slightly lower as to susceptible cells. C4 binding studies, however, revealed that the observed difference in **antibody** and C1q binding has no influence on the complement resistance of SK-MEL-170 cells: significantly more C4b was bound to complement-resistant (1565 .+-. 92 fg/cell) as compared to susceptible cells (715 .+-. 31 fg/cell). On extraction of the molecular forms of C4 bound to the cell membranes, an additional high molecular weight C4 species-apparently a C4b-C4b homodimer-appeared

only on the resistant SK-MEL-170 cells that may function as a residual back-up **C5** convertase. Collectively, these results show that SK-MEL-170 human melanoma cells evade complement-mediated cytolysis despite sufficient activation of early components of the classical complement pathway by p65-mediated rapid degradation of surface-bound C3b, leading to a significant reduction in membrane attack complex formation. Thus, rapid cleavage of surface deposited C3b was established as a powerful mechanism of complement resistance.

L16 ANSWER 4 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 92:477083 BIOSIS
DN BA94:108458
TI FORMATION AND STRUCTURE OF THE C5B-7 COMPLEX OF THE LYTIC PATHWAY OF COMPLEMENT.
AU DISCIPIO R G
CS DEP. IMMUNOLOGY IMM18, RESEARCH INSTITUTE SCRIPPS CLINIC, 10666 N. TORREY PINES RD., LA JOLLA, CALIF. 92037.
SO J BIOL CHEM 267 (24). 1992. 17087-17094. CODEN: JBCHA3 ISSN: 0021-9258
LA English
AB The formation and structure of the complement cytolytic intermediary complex, C5b-7, were studied with the aim of determining the interactive regions of **C5**, C6, and C7. The structure of human complement component **C5** was elucidated by the application of limited proteolysis which generated well characterized major polypeptide fragments of this molecule. Plasmin, thrombin, and kallikrein cleave C5b with greater facility than **C5**. The most useful cleavage of C5b was effected by plasmin because the fragmentation pattern was similar to the processing the C3b by factors H, I, and kallikrein. Plasmin hydrolyzes peptide bonds within the **.alpha.'-chain** of C5b, resulting in a four-chain fragment, C5c (Mr = 142,000), and a single chain fragment, C5d (Mr = 43,000). Circular dichroism spectroscopic analyses indicated that C5d is substantially richer in .alpha.-helical content than is C5c (27 versus 9%). Polyclonal **antibodies** directed against C5c blocked the interaction of C5b-6 with C7, whereas **antibodies** directed against C5d inhibited the binding of **C5** with C3b. Chemical cross-linking using a cleavable radioiodinated photoreactive reagent revealed that both C6 and C7 associate preferentially with the **.alpha.'-chain** of C5b. The reversible interactions of **C5** with C6, C7, and major polypeptide fragments derived from these were investigated with solid phase binding assays. The results indicate that the carboxyl-terminal domains of C6 and C7, which have cysteine-rich modules homologous to those found in factors H and I, have the capacity to link specifically with **C5**.

L16 ANSWER 5 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 92:28069 BIOSIS

DN BA93:17344
TI AMINO ACID RESIDUES 1101-1105 OF THE ISOTYPIC REGION OF HUMAN C4B IS IMPORTANT TO THE COVALENT BINDING ACTIVITY OF COMPLEMENT COMPONENT C4.
AU REILLY B D; LEVINE R P; SKANES V M
CS FACULTY MEDICINE, MEMORIAL UNIVERSITY NEWFOUNDLAND, ST. JOHN'S, NFLD. CAN. A18 3V6.
SO J IMMUNOL 147 (9). 1991. 3018-3023. CODEN: JOIMA3 ISSN: 0022-1767
LA English
AB The C4A and C4B isotypes of human C4 show certain functional differences that stem from their relative preference for transacylation to amino (-NH2) vs hydroxyl (-OH) nucleophiles, respectively, on complement-activating surfaces. Comparison of amino acid sequences of the .**alpha**.-**chain** fragment of C4, C4d, has shown C4A- and C4B-specific sequences at residues 1101-1106 are the only consistent structural difference between isotype, i.e., Pro, Cys, Pro, Val, Leu, Asp in C4A and Leu, Ser, Pro, Val, Ile, His in C4B. These residues may be responsible either in part or entirely for properties associated with isotype. To examine the functional role of residues 1101-1106 in C4B-mediated hemolysis, whole serum or immunopurified human C4 with allotypes, A3B1, A3, B2B1, or B1 were preincubated in the presence or absence of an antipeptide mAb (BII-1) specific for amino acid residues 1101-1105 of C4B. Sensitized sheep E and C4-deficient guinea pig serum was then added and lysis measured by absorbance at 415 nm. Our results show lysis of **antibody**-sensitized sheep E is inhibited by **antibody** and C4B2B1, C4B1, or C4A3B1 but not **antibody** and C4A3. The interference of hemolysis by BII-1 could not be explained by inhibition of activation of C4B or inhibition of C3 or **C5** convertase activity. Furthermore, results from uptake experiments show that BII-1 interferes with the covalent binding activity of C4B, indicating residues 1101-1105 play a role in the covalent binding reaction of C4B to the target E-**antibody** complex.

L16 ANSWER 6 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 91:409305 BIOSIS
DN BA92:76270
TI A COVALENT DIMER OF COMPLEMENT C4B SERVES AS A SUBUNIT OF A NOVEL **C5** CONVERTASE THAT INVOLVES NO C3 DERIVATIVES.
AU MASAKI T; MATSUMOTO M; YASUDA R; LEVINE R P; KITAMURA H; SEYA T
CS DEP. IMMUNOLOGY, CENTER ADULT DISEASES, OSAKA, HIGASHINARI-KU, OSAKA 537, JPN.
SO J IMMUNOL 147 (3). 1991. 927-932. CODEN: JOIMA3 ISSN: 0022-1767
LA English
AB A C intermediate, LAC14, was prepared from TNP-aminocaproyl liposomes sensitized with anti-TNP **antibody** (Ab) and purified human C1 and C4. LAC14, containing radiolabeled C4, was analyzed by SDS-PAGE followed by autoradiography, and yielded a 210-kDa band and

a predominant 400-kDa band. The 210-kDa band consisted of monomeric C4b bound to low molecular mass acceptors. The 400-kDa band was comprised of a 200-kDa moiety, as well as .beta.- and .gamma.-chains of C4. The 200-kDa moiety contained neither C1 nor sensitizing Ab, but it was largely decreased by treatment with NH2OH to the 90-kDa moiety with the mobility corresponding to the .**alpha**.'-**chain** of C4b. A covalent dimer of C4b, therefore, is the predominant form of C4b deposited on liposomes sensitized with **antibody**. The C4b-C4b dimer formed rapidly (within 5 min) followed by slow dissociation into monomers. The LAC14 bearing the C4b dimer but not the monomer was lysed, although with relatively low efficiency, by the addition of oxyC2 and EDTA-supplemented C3-deficient serum (C3DS), and, furthermore, LAC142 possessed the ability to convert **C5** into C5a and C5b. Moreover, lysis was inhibited not by anti-C3 Ab but by anti-C4 Ab. In other experiments, the dimer served as an element of C3 convertase, as well. These findings imply that the C4b dimer, when complexed with C2, expresses C3/**C5** convertase activity without participation of C3, and may provide a molecular mechanism whereby sera from patients with complete C3 deficiency retain the ability to induce C-mediated cytolysis.

L16 ANSWER 7 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 91:223315 BIOSIS
DN BA91:114775
TI STRUCTURAL AND FUNCTIONAL COMPARISON OF TYPE IX COLLAGEN PROTEOGLYCAN FROM CHICKEN CARTILAGE AND VITREOUS HUMOR.
AU BREWTON R G; WRIGHT D W; MAYNE R
CS DEP. CELL BIOL., UNIV. ALABAMA AT BIRMINGHAM, UAB STATION-BOX 302, BIRMINGHAM, ALA. 35294.
SO J BIOL CHEM 266 (8). 1991. 4752-4757. CODEN: JBCHA3 ISSN: 0021-9258
LA English
AB Type IX collagen-proteoglycan is a major component of hyaline cartilages where it is located on the surface of the collagen fibrils so that a collagenous domain of the molecule (called COL3) and a non-collagenous domain (called NC4) project at periodic distances away from the surface of the fibril. Type IX collagen-proteoglycan is also present on the surface of the collagen fibrils of the adult chicken vitreous but, unlike cartilage, lacks the NC4 domain and possesses a very long chondroitin sulfate chain which provides an extensive coat to the fibril. A monoclonal **antibody** (called 4D6) is described which will distinguish cartilage from vitreous type IX collagen. To form the epitope for 4D6 two peptides called C2 and **C5** derived, respectively, from the .alpha.1(IX) and .**alpha**.3(IX) **chains** are required. Further analysis shows that specificity for 4D6 resides only in the C23 peptide from cartilage and not in **C5**. These results are entirely consistent with recent evidence that there are two promoters for transcription of the .**alpha**.1(IX) **chain** which

will result in an .**alpha**.1(IX) **chain** in which the NC4 domain is either present or absent and that expression of these two promoters has tissue specificity (Nishimura, I., Muragaki, Y., and Olsen, B. R. (1989) J. Biol. Chem. 264, 20033-20041). In addition, the function of type IX collagen in cartilage and vitreous may differ with the long chondroitin sulfate chains of vitreous type IX collagen being responsible for the gel-like matrix of this tissue.

L16 ANSWER 8 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 89:448305 BIOSIS
DN BA88:96577
TI RAPID ISOLATION AND CHARACTERIZATION OF NATIVE MOUSE COMPLEMENT COMPONENTS C3 AND **C5**.
AU VAN DEN BERG C W; VAN DIJK H; CAPEL P J A
CS ACADEMIC HOSP. UTRECHT, LAB. MICROBIOL., POSTBUS 85500, 3508 GA UTRECHT, NETHERLANDS.
SO J IMMUNOL METHODS 122 (1). 1989. 73-78. CODEN: JIMMBG ISSN: 0022-1759
LA English
AB A rapid, 1 day procedure for the purification of mouse complement factors C3 and **C5** is described. The method is based on fractionated precipitation by polyethylene glycol 6000, followed by MonoQ anion exchange chromatography on a system for fast protein liquid chromatography (FPLC). For C3 isolation, an additional FPLC separation step using Superose 12 (gel filtration) was used. C3 was purified 71-fold with a yield of 32% as measured by biological activity; the preparation contained no detectable contaminants as judged by SDS-PAGE. A comparable procedure for the isolation of **C5** resulted in a preparation with a considerable contamination which could be easily removed by affinity chromatography using **antibodies** directed against these contaminants. With this combined procedure **C5** was purified 536-fold with a yield of 28% based on biological activity. SDS-polyacrylamide gel electrophoresis revealed that mouse C3 and **C5** had apparent Mrs of 170,000 and 190,000, respectively. Under reducing conditions the .**alpha**. and .beta. **chains** showed Mrs of 107,000 and 62,000 for C3, and 104,000 and 85,000 for **C5**.

L16 ANSWER 9 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 88:482712 BIOSIS
DN BA86:114022
TI ANALYSIS OF HUMAN C8 WITH MONOCLONAL **ANTIBODIES** CHARACTERIZATION OF A MONOCLONAL **ANTIBODY** THAT RECOGNIZES FREE C8-ALPHA-GAMMA SUBUNIT.
AU DOGLIO L T; GAWRYL M S; LINT T F
CS DEP. IMMUNOL./MICROBIOL., RUSH-PRESBYTERIAN-ST. LUKE'S MED. CENT., CHICAGO, ILLINOIS 60612.
SO J IMMUNOL 141 (6). 1988. 2079-2083. CODEN: JOIMA3 ISSN: 0022-1767

LA English
AB The eighth component of human C is essential for the formation of the membranolytic C attack complex. C8 has a unique structure in that two covalently linked **chains**, C8.**alpha**. and C8.gamma., are associated non-covalently with the third chain, C8.beta.. In order to study the structure and assembly of the C8 molecule, a panel of mAb has been produced against the C component C8. Eight of these mAb had reactivity to the C8.alpha.-.gamma. subunit, whereas four reacted with C8.beta.. One of the C8.alpha.-.gamma. mAb, C8A2, had specificity for an epitope on the C8.**alpha**.-**chain** and exhibited no cross-reactivity to any of the other terminal C components, including C8.beta.. C8A2 inhibited the hemolytic activity of the C8.alpha.-.gamma. subunit but had no effect on the activity of fluid phase whole C8 or C8 within membrane-bound C5b8. Functional experiments suggest that C8A2 inhibits C8.alpha.-.gamma. activity by interfering with its interaction with the C8.beta.-chain. In an enzyme immunoassay using the C8A2 mAb, free C8.alpha.-.gamma. subunit could be detected in both homozygous and heterozygous C8.beta.-deficient serum. However, only low level binding was observed when homozygous **C5**- and C7-deficient sera were tested. Thus the mAb, C8A2, recognizes an epitope expressed on the C8.alpha.-.gamma. subunit but not on intact C8 and can detect free C8.alpha.-.gamma. in the presence of native C8.

L16 ANSWER 10 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 88:331418 BIOSIS
DN BA86:37969
TI USE OF ANTISERA TO THE ISOLATED ALPHA AND BETA SUBUNITS OF C3 AS PROBES TO STUDY FUNCTIONAL SITES PRESENT ON PARTICLE-BOUND C3B BUT ABSENT ON NATIVE SOLUBLE FORMS OF C3.
AU WHALEY K; NILSSON U
CS BLOOD CENTRE, UNIV. HOSP., S-751 85 UPPSALA, SWEDEN.
SO INT ARCH ALLERGY APPL IMMUNOL 86 (1). 1988. 55-61. CODEN: IAAAAM ISSN: 0020-5915
LA English
AB The effect of antisera to the isolated .**alpha**. and .beta. **chains** of C3 on certain C3b-dependent reactions has been studied. **C5**-mediated haemolysis of EAC1423b was inhibited preferentially by antiserum to the .**alpha**. **chain**, whereas antiserum to the .beta. chain inhibited the formation of C3bBb. The anti-.beta. chain antiserum also stabilised C3bBbP, and rendered the enzyme relatively resistant to accelerated decay in the presence of factor H. These and previous findings that anti-.alpha. and anti-.beta. IgG bind to restricted subsets of antigenic determinants on C3/C3b suggest that these antisera affect C3b function through the binding of **antibodies** to active binding sites exclusively exposed by bound C3b. The anti-.alpha. and anti-.beta. **antibody** probes are currently being further

developed to verify this interpretation.

L16 ANSWER 11 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 87:359289 BIOSIS
DN BA84:56692
TI TRYPANOSOMA-LEWISI RESTRICTION OF ALTERNATIVE COMPLEMENT PATHWAY C3-**C5** CONVERTASE ACTIVITY.
AU STURTEVANT J E; BALBER A E
CS DIV. IMMUNOL., DEP. MICROBIOL. AND IMMUNOL., DUKE UNIVERSITY MED. CENT., P.O. BOX 3010, DURHAM, N.C. 27710, USA.
SO EXP PARASITOL 63 (3). 1987. 260-271. CODEN: EXPAAA ISSN: 0014-4894
LA English
AB The rat parasite Trypanosoma lewisi was incubated in vitro with rat or human serum, washed, and extracted in detergent. Extracts were fractionated by electrophoresis in denaturing gels, transferred to nitrocellulose, allowed to renature, then immunoblotted with polyclonal **antibodies** to rat complement component C3 and human complement components C3, **C5**, and factor B. Molecules that reacted with these **antibodies** were detected in the extracts. Fragments of rat C3 were detected in extracts of parasites that had not been exposed to serum in vitro. Additional complement deposition occurred during in vitro incubations; human complement components deposited in vitro could be distinguished from rat components deposited in vivo. Complement deposition in vitro required magnesium ions and did not occur when heat inactivated serum was used. Components reacting with **antibodies** to human C3 included a group of bands with molecular weights higher than C3. **alpha**. or .beta. **chains**. Blotting with affinity purified, chain specific **antibodies** demonstrated that a 68 kDa component on parasites is C3.beta. and that a 44 kDa molecule is derived from C3.alpha.. A 73 kDa component that was difficult to resolve from C3.beta. is probably also a C3.alpha. fragment. This suggests that an inactive iC3b-like molecule is present on parasites. Kinetic studies showed that cleavage of C3.alpha. is rapid and that the amount of C3.alpha. fragments and C3.beta. on intact parasites reached a steady state after 15 min. When parasites were trypsinized prior to incubation in **C5** or C6 deficient serum, the rate and extent of C3 and **C5** deposition increased. Unprocessed C3.alpha.' and **C5.alpha.' chains** were detected. Trypsinized parasites were lysed by the alternative complement pathway in normal serum. Intact parasites could be lysed by complement in the presence of **antibody**. The data support our previous suggestion that trypsin sensitive surface proteins on intact T. lewisi limit alternative pathway activity by restricting C3/**C5** convertase activity.

L16 ANSWER 12 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 87:337772 BIOSIS
DN BA84:46715

TI FUNCTIONAL ANALYSIS AND QUANTIFICATION OF THE COMPLEMENT C3 DERIVED ANAPHYLATOXIN C3A WITH A MONOCLONAL **ANTIBODY**.
AU BURGER R; BADER A; KIRSCHFINK M; ROTHER U; SCHROD L; WOERNER I; ZILOW G
CS INST. IMMUNOL., IM NEUENHEIMER FELD 305, 6900 HEIDELBERG, W. GER.
SO CLIN EXP IMMUNOL 68 (3). 1987. 703-711. CODEN: CEXIAL ISSN: 0009-9104
LA English
AB The C3 fragment C3a belongs to the anaphylatoxins. It has immune regulatory activity and contributes to the pathogenesis of the adult respiratory distress syndrome (ARDS). The low molecular weight (9 kD) of C3a complicates the production of **antibodies** to C3a. We obtained a monoclonal **antibody** (designated H13) to human C3a. It reacts with C3a or C3a-desArg and with native C3 but not with **C5** or C5a. In immunoblot analysis it reacts with the .alpha.- but not with .beta.-chain of C3 and binds to a protein with a mol. wt of about 10 kD present in zymosan-activated sera which is only marginally detectable in non-activated serum and absent in plasma. H13 crossreacts with the analogous proteins of rabbit, guinea pig and sheep. H13 has the capacity to bind 125I-radiolabelled C3a efficiently but fails totally to react with 125I-C5a or with other C3 .**alpha**.-**chain** fragments, H13 blocks C3a functional activity. It markedly inhibits C3a-induced 3H-serotonin release from platelets in vitro and similarly inhibits the C3a-induced extravasation of Evans blue into the skin in vivo. H13 does not interfere with the haemolytic activity of C3. An ELISA system was established using H13 which permits quantification of C3a in sera of polytrauma patients. The **antibody** H13 should facilitate further functional analysis of C3a in experimental systems. It should be useful for quantification of C3a in diagnostic assays and also for application in immunopathology.

L16 ANSWER 13 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 87:337585 BIOSIS
DN BA84:46528
TI COVALENT ASSOCIATION OF C3B WITH C4B WITHIN **C5** CONVERTASE OF THE CLASSICAL COMPLEMENT PATHWAY.
AU TAKATA Y; KINOSHITA T; KOZONO H; TAKEDA J; TANAKA E; HONG K; INOUE K
CS DEP. BACTERIOLOGY, OSAKA UNIV. MED. SCH., SUITA, OSAKA 565, JAPAN.
SO J EXP MED 165 (6). 1987. 1494-1507. CODEN: JEMEAV ISSN: 0022-1007
LA English
AB The C convertase of the classical complement pathway is a complex enzyme consisting of three complement fragments, C4b, C2a, and C3b. Previous studies have elucidated functional roles of each subunit (4, 6, 7), but, little is known about how the subunits associate with each other. In this investigation, we studied the nature of the classical C% convertase that was assembled on sheep erythrocytes. We found that one of the nascent C3b molecule that had been generated by the C3 convertase directly bound covalently to C4b. C3b bound to the

.alpha.' chain of C4b through an ester bond, which could be cleaved by treatment with hydroxylamine. The ester bond was rather unstable, with a half-life of 7.9 h at pH 7.4 and 37% C. Formation of the C4b-C3b dimer is quiet efficient; e.g., 54% of the cell-bound C3b was associated with C4b when 25,000 molecules of C4b and 12,000 molecules of C3b were present per cell. Kinetic analysis also showed the efficient formation of the C4b-C3b dimer; the rate of dimer formation was similar to or even faster than that of cell-bound monomeric C3b molecules. These results indicate that the C4b is a highly reactive acceptor molecule for nascent C3b. High-affinity **C5**-binding site with an association constant of 2.1 .times. 108 L/M were demonstrated on C4b-C3b dimer-bearing sheep erthocytes, EAC43 cells. The number of high-affinity **C5** -binding sites coincided with the number of C4b-C3b dimers, but not with the total number of cell-bound C3b molecules. Anti-C4 **antibodies** caused 80% inhibition of the binding of **C5** to EAC43 cells. These results suggest that only C4b-associated C3b serves as a high-affinity **C5** binding site. EAC14 cells had a small amount of high-affinity **C5** binding sites with an association constant of 8.1 .times. 107 L/M 100 molecules of bound C4b being necessary for 1 binding site. In accordance with the hypothesis that C4b-associated C4b might also serve as a high-affinity **C5**-binding site, a small amount of C4b-C4b dimer was detected on EAC14 cells by SDS-PAE analysis. Taken together, these observations indicate that high-affinity binding of **C5** is probably divalent, in that **C5** recognizes both promoters with dimers. The high-affinity binding may allow selective binding of **C5** to the convertase in spite of surrounding monomeric C3b molecules.

L16 ANSWER 14 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 84:339305 BIOSIS
DN BA78:75785
TI RESIDUAL HEMOLYTIC AND PROTEOLYTIC ACTIVITY EXPRESSED BY BB AFTER DECAY DISSOCIATION OF C-3B BB.
AU FISHELSON Z; MULLER-EBERHARD H J
CS DEPARTMENT OF IMMUNOLOGY, RESEARCH INSTITUTE OF SCRIPPS CLINIC, LA JOLLA, CALIF. 92037.
SO J IMMUNOL 132 (3). 1984. 1425-1429. CODEN: JOIMA3 ISSN: 0022-1767
LA English
AB Bb [factor B, fragment b] (MW = 63,000) is the catalytic site-bearing subunit of the C3 [complement component 3] convertase of the alternative complement pathway, C3b,Bb, which is dissociated from the complex upon decay of the enzyme. Because purified Bb induced certain leukocyte activities, it was examined whether it expresses residual hemolytic or proteolytic activity. Hemolytic activity of Bb was tested by using Factor B- or Factor D-depleted normal human serum and rabbit or sheep erythrocytes. Proteolytic activity of Bb was assessed by using purified C3 or **C5** as substrates and SDS-PAGE

[sodium dodecyl sulfate-polyacrylamide gel electrophoresis] to detect protein cleavage. Bb expressed metal-dependent hemolytic activity that was .apprx. 100-fold lower than that of Factor B. This activity could be inhibited by Factor H and enhanced by properdin. Low but statistically significant binding of 125I-labeled Bb to C3b on erythrocytes was demonstrated. Monoclonal **antibodies** that bind to Bb but not to intact Factor B inhibited the Bb hemolytic activity. Purified Bb cleaved C3 to C3a and C3b, as evidenced by the appearance of the .**alpha**.'-**chain** of C3b. It also cleaved **C5** to C5a and C5b when cobra venom factor [CVF] was present in the reaction mixture. Metal ions were required for expression of proteolytic activity, and Ni supported the activity better than Mg. Decayed Bb has residual C3 and **C5** cleaving activity and hemolytic activity, expression of which appears to require its association with C3b, C3(H2O), or CVF. These observations may aid in explaining the mechanism of action of Bb on leukocytes.

L16 ANSWER 15 OF 15 BIOSIS COPYRIGHT 1995 BIOSIS
AN 82:150280 BIOSIS
DN BA73:10264
TI COMPLEMENT RECEPTOR IS AN INHIBITOR OF THE COMPLEMENT CASCADE.
AU IIDA K; NUSSENZWEIG V
CS DEP. PATHOL., N.Y. MED. CENT., NEW YORK, 10016, USA.
SO J EXP MED 153 (5). 1981. 1138-1150. CODEN: JEMEAV ISSN: 0022-1007
LA English
AB A glycoprotein from the membrane of human erythrocytes was identified as a receptor for C3b (b fragment of complement component 3) (CR1). It promotes the dissociation of the alternative pathway C3 convertase C3b,Bb and the cleavage of C3b by C3b/C4b inactivator. CR1 also inactivates the C3 and **C5** convertases of the classical pathway. CR1 inhibits the consumption of C3 by C3 convertase EAC142 (sheep erythrocyte-**antibody**-complement complex) and enhances the decay of C4b,2a sites. On a weight basis, CR1 is 5-10 times more active than C4 binding protein, a serum inhibitor of C4b,2a. The binding of 125I-CR1 to EAC14 cells is inhibited by C2. CR1 and C2 probably compete for a site on C4b. CR1 inhibited **C5** convertase even more effectively, but had no effect on the assembly of the late complement components. At high concentrations, CR1 alone has no irreversible effects on cell-bound C4b. In the fluid phase, CR1 can function as a cofactor for the cleavage of the .**alpha**.' **chain** of C4b by C3b/C4b inactivator. A well-known function of CR1 is to promote adherence of microbes or immune complexes bearing C3b and C4b to cells. This interaction could result in a microenvironment damaging to the plasma membrane of the responding cell because the extrinsic C3b and C4b fragments can serve as additional sites of assembly of enzymes of the cascade. CR1 on the surface of cells may supply an increased local concentration of a strong inhibitor of the amplifying enzymes of the complement system and may provide cells with a mechanism for circumventing damage when

they bind C3b- and C4b-bearing substrates.

L23 ANSWER 1 OF 1 BIOSIS COPYRIGHT 1995 BIOSIS
AN 93:95308 BIOSIS
DN BA95:50504
TI STREPTOCOCCAL **C5A** PEPTIDASE IS A HIGHLY SPECIFIC ENDOPEPTIDASE.
AU CLEARY P P; PRAHBU U; DALE J B; WEXLER D E; HANDLEY J
CS DEP. MICROBIOL., UNIV. MINN., MINNEAPOLIS, MINN. 55455, USA.
SO INFECT IMMUN 60 (12). 1992. 5219-5223. CODEN: INFIBR ISSN: 0019-9567
LA English
AB Compositional analysis of streptococcal **C5a** peptidase (SCPA) cleavage products from a synthetic peptide corresponding to the 20 C-terminal residues of **C5a** demonstrated that the target **cleavage site** is His-Lys rather than Lys-Asp, as previously suggested. A **C5a** peptide analog with Lys replaced by Gln was also subject to cleavage by SPCA. This confirmed that His-Lys rather than Lys-Asp is the scissile bond. Cleavage at histidine is unusual but is the same as that suggested for a peptidase produced by group B streptococci. Native C5 protein was also resistant to SPCA, suggesting that the His-Lys bond is inaccessible prior to proteolytic cleavage by C5 convertase. These experiments showed that the streptococcal **C5a** peptidase is highly specific for **C5a** and suggest that its function is not merely to process protein for metabolic consumption but to act primarily to eliminate this chemotactic signal from inflammatory foci.

=> fil hca
FILE 'HCA' ENTERED AT 10:33:03 ON 29 JUN 95
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=> d his l24-

(FILE 'HCA' ENTERED AT 10:30:28 ON 29 JUN 95)
L24 0 S (C5A (L)CLEAVAGE SITE#)
L25 2 S (C5A (L)CLEAVAGE SITE#)/AB

FILE 'BIOSIS' ENTERED AT 10:31:27 ON 29 JUN 95

FILE 'HCA' ENTERED AT 10:33:03 ON 29 JUN 95

=> d bib ab 1-2

L25 ANSWER 1 OF 2 HCA COPYRIGHT 1995 ACS
AN 118:142332 HCA
TI Streptococcal C5a peptidase is a highly specific endopeptidase
AU Cleary, P. Patrick; Prahbu, Usha; Dale, James B.; Wexler, Daniel E.; Handley, Jeffrey
CS Dep. Microbiol., Univ. Minnesota, Minneapolis, MN, 55455, USA
SO Infect. Immun. (1992), 60(12), 5219-23
CODEN: INFIBR; ISSN: 0019-9567
DT Journal
LA English
AB Compositional anal. of streptococcal **C5a** peptidase (SCPA) cleavage products from a synthetic peptide corresponding to the 20 C-terminal residues of **C5a** demonstrated that the target **cleavage site** is His-Lys rather than Lys-Asp, as previously suggested. A **C5a** peptide analog with Lys replaced by Gln was also subject to cleavage by SCPA. This confirmed that His-Lys rather than Lys-Asp is the scissile bond. Cleavage at His is unusual but is the same as that suggested for a peptidase produced by group B streptococci. Native C5 protein was also resistant to SCPA, suggesting that the His-Lys bond is inaccessible prior to proteolytic cleavage by C5 convertase. These expts. showed that the streptococcal **C5a** peptidase is highly specific for **C5a** and suggest that its function is not merely to process protein for metabolic consumption but to act primarily to eliminate this chemotactic signal from inflammatory foci.

L25 ANSWER 2 OF 2 HCA COPYRIGHT 1995 ACS
AN 104:146822 HCA
TI Parameters of the stimulation of human monocytes by factor B of the complement system
AU Baumgarten, H.; Opperman, M.; Schulze, M.; Goetze, O.
CS Zent. Hyg. Humangenet., Universitaetsklin. Goettingen, Goettingen, D-3400, Fed. Rep. Ger.
SO Mononucl. Phagocytes, [Proc. Conf.], 4th (1985), Meeting Date 1984, 163-71. Editor(s): Van Furth, Ralph. Publisher: Nijhoff, Dordrecht, Neth.
CODEN: 54WAAX
DT Conference
LA English
AB Evidence is provided for a complement factor B (Bb)-dependent stimulation of human monocytes with respect to the secretion of lysosomal hydrolases and H2O2 and to receptor-mediated phagocytosis. It is further demonstrated that divalent antibody mols. specific for the **C5a** region of the .alpha.-chain of C5 are able to induce the secretion of lysosomal hydrolases in the absence of any

other added stimulus. Probably membrane-assocd. (m)C5 is oriented in the monocyte plasma membrane in such a way that the **C5a** portion of its .alpha.-chain is accessible to antibody added to the outside of the cell. Apparently, the **cleavage site** for Bb on the .alpha.-chain of mC5 is externally disposed, so the obsd. effects of Bb on human monocytes are caused by the generation of mC5 and **C5a**.

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=> fil wpids
FILE 'WPIDS' ENTERED AT 10:36:50 ON 29 JUN 95
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FILE LAST UPDATED: 26 JUN 95                <950626/UP>
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MOST RECENT DERWENT WEEK             9524   <199524/DW>
DERWENT WEEK FOR CHEMICAL CODING:    9514
DERWENT WEEK FOR POLYMER INDEXING:   9518
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE
>>> DERWENT POLYMER INDEXING THESAURUS AVAILABLE IN FIELD /PLE <<<
     >>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<
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>>>NOW AVAILABLE - NEW USER MANUAL GLOBAL PATENT SOURCES - SEE NEWS<<<

=> d his l26-

     (FILE 'BIOSIS' ENTERED AT 10:31:27 ON 29 JUN 95)

     FILE 'HCA' ENTERED AT 10:33:03 ON 29 JUN 95

     FILE 'WPIDS' ENTERED AT 10:33:20 ON 29 JUN 95
L26           1 S 5G1 OR 5G1 1 OR 5G11 OR 5G46K OR 5G27K OR 5G200## OR KS
L27           3 S C5 (L) (NEPHRITIS OR GLOMERULONEPHRIT?)
L28           1 S C5 (L) ALPHA CHAIN#
L29           0 S C5A (L) CLEAVAGE SITE#
L30           0 S C5A (L) CLEAVAGE

     FILE 'WPIDS' ENTERED AT 10:36:50 ON 29 JUN 95

=> d bib l26;d bib ab l27 1-3;d bib ab l28

L26  ANSWER 1 OF 1  COPYRIGHT 1995 DERWENT INFORMATION LTD
AN   95-164747 [22]   WPIDS
DNN  N95-129265
TI   CRT with lengthened stem pins near neck end - applies high pressure
     on projected part near the end face of the neck to raise break down
     voltage.
DC   V05
PA   (SONY) SONY CORP
CYC  1
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PI JP 07085821 A 950331 (9522)* 4 pp
ADT JP 07085821 A JP 93-231866 930917
PRAI JP 93-231866 930917

L27 ANSWER 1 OF 3 COPYRIGHT 1995 DERWENT INFORMATION LTD
AN 95-138960 [18] WPIDS
CR 92-234284 [28]; 93-017593 [02]
DNC C95-064230
TI Compsn. for treating immune or complement-medicated disorders - contains 4-substd. spiro-benzofuran-2(3H)-cyclohexane deriv., e.g. for treating adult respiratory distress syndrome.
DC B02
IN BRADBURY, B J; IP, S H; KAUFMAN, T; MARSH, H C; SINDELAR, R D
PA (TCEL-N) T CELL SCI INC; (UMIS) UNIV MISSISSIPPI
CYC 1
PI US 5401767 A 950328 (9518)* 36 pp
ADT US 5401767 A Div ex US 88-182275 880415, US 92-997266 921221
FDT US 5401767 A Div ex US 5173499
PRAI US 88-182275 880415; US 92-997266 921221
AB US 5401767 A UPAB: 950518
A pharmaceutical compsn. for treating immune disorders or disorders involving undesirable or inappropriate complement activity, contains a 4-(hydroxy or alkoxy)-spiro -(benzofuran-2(3H)- cyclohexane) deriv. of formula (I) or its salt; R = H or lower alkyl; R1 = H, COOH, CHO, CH2OH, N-(lower alkyl)-carboxamido-, COCF3, alkoxycarbonyl, halide, 2-10C substd. vinyl or 2-20C alkylidene (sic); R2 = H, COOH, CHO, CH2OH, halide, 2-10 substd. vinyl or 2-20C alkylidene (sic); provided that one of R1 and R2 is H when the other is other than H.

In another claim for such compsns. R2 is undefined and no provisos are given.

USE - (I) have complement inhibiting activity; esp. they selectively inhibit complement at the **C5** stage of actuation and block release of C5a.

(I) also have immunosuppressant activities, eg, by inhibiting natural killer activity, lymphocyte proliferation and T-cell actuation.

They are useful for combatting inflammatory and/or immune disorders. Conditions treated include: rheumatoid arthritis, acute gouty arthritis and acute immunological arthritis; pulmonary disorders such as adult respiratory distress syndrome, pulmonary dysfunction due to haemodialysis, chronic progressive pulmonary dis-cystic fibrosis, byssinosis or asbestos-induced inflammation; inflammation due to systemic lupus erythematosus; kidney stones, multiple sclerosis or **glomerulonephritis**; Purscher's retinopathy; haemorrhagic pancreatitis; renal cortical necrosis; primary biliary cirrhosis inflammatory; nephro-pathology; cranial

nerve damage in meningitis; tumour cell metastasis; extended tissue destruction in myocardial infarction or burns; tissue damage due to myocardial ischaemia and reperfusion; atrophic gastoitis; thyroiditis; allergic encephalomyelitis; gastric mucosa disorders; thyrotoxicosis; autoimmune haemolytic anaemia; pemphigus vulgaris; sympathetic ophthalmia; delayed-type hypersensitivity; allograft or organ transplant rejection; graft-host reaction; other autoimmune disorders; drug allergies; and adverse effects of complement actuation caused by therapeutic intervention such as tissue plasminogen activator therapy or cardio-pulmonary by-pass.

(I) may be administered orally or parenterally. No dosage ranges are given.

Dwg.0/7

L27 ANSWER 2 OF 3 COPYRIGHT 1995 DERWENT INFORMATION LTD
AN 92-234373 [28] WPIDS
TI Synergistic compsn. of biological and non-protein organic cpds. - inhibiting soluble complement receptor and/or having immunosuppressive activity, for treating immune and inflammatory disorders e.g. arthritis.
DC B02 B04 D16
IN KUNG, P C; MARSH, H C
PA (TCEL-N) T CELL SCI INC
CYC 20
PI WO 9210205 A1 920625 (9228)* 100 pp
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
W: AU CA JP KR US
AU 9191497 A 920708 (9241)
EP 560929 A1 930922 (9338) EN
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
JP 06503344 W 940414 (9420) 28 pp
ADT WO 9210205 A1 WO 91-US9300 911206; AU 9191497 A AU 91-91497 911206, WO 91-US9300 911206; EP 560929 A1 WO 91-US9300 911206, EP 92-902709 911206; JP 06503344 W WO 91-US9300 911206, JP 92-502865 911206
FDT AU 9191497 A Based on WO 9210205; EP 560929 A1 Based on WO 9210205; JP 06503344 W Based on WO 9210205
PRAI US 90-623878 901206
AB WO 9210205 A UPAB: 931025
Compsn. comprises: (a) a biological cpd. (I) inhibiting activity of complement; and (b) a non-protein organic cpd. (II) having immunosuppressive, complement inhibiting or antiinflammatory activity. Molecule comprises (I) covalently linked to (II). Compsn. comprises (a) a soluble CR1 fragment lacking a transmembranme region which has functional activity of CR1 in vitro to inhibit complement-mediated haemolysis, to inhibit C3a and/or C5a prodn. to bind C3b and C4b, to show factor I cofactor activity, and to inhibit C3 and/or **C5** convertase activity; and (b) 6-carboxy-7-formyl-4-methoxy spiro (benzofuran-2(3h)-cyclohexane).

USE - Used for immune-complex-induced vasculitis, arthritis

type II collagen-induced- or acute immunological arthritis, myasthemia gravis, acute gouting arthritis, systemic lupus erythematosis, haemolytic anaemia, multiple sclerosis, **glomerulonephritis**, and experimental allergic neuritis; immune complex- or; pulmonary- disorders e.g. adult respiratory distress syndrome, pulmonary dysfunction-haemodialysis, chronic progressive pulmonary dis-cystic fibrosis, byssinosis, and asbestos-induced inflammation; inflammation of **glomerulonephritis** or Crohn's disease; Purtscher's retinopathy; haemorrhagic pancreatitis; renal cortical necrosis; primary biliary cirrhosis inflammation; nephropathology; cranial nerve damage in meningitis; tumour cell metastasis; extended tissue destruction in myocardial infarction or burns; infectious disease induced by virus e.g. Epstein-Barr Virus Associated diseases, Sjogren's syndrome, rheumatoid arthritis, Urkitt's lymphoma, Hodgkins disease, AIDS or EBV associated B cell lymphoma, chronic fatigue syndrome, parasitic diseaes states (e.g. viral infection following allograft transplantation or AIDS); and HTLV-III/LAV/HIV. Dwg.0/3

L27 ANSWER 3 OF 3 COPYRIGHT 1995 DERWENT INFORMATION LTD
AN 92-234284 [28] WPIDS
CR 93-017593 [02]; 95-138960 [18]
DNC C92-105622
TI Spiro-benzo-di-hydro-furan-2(3H)-cyclohexane derivs. - inhibit complement and/or suppress immune activity.
DC B02
IN BRADBURY, B J; IP, S H; KAUFMAN, T S; LEE, C; MARSH, H C; SINDELAR, R D
PA (TCEL-N) T CELL SCI INC; (UMIS) UNIV MISSISSIPPI
CYC 20
PI WO 9210096 A1 920625 (9228)* EN 112 pp
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE
W: AU CA JP KR US
AU 9191274 A 920708 (9241)
EP 561989 A1 930929 (9339) EN
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
JP 06503829 W 940428 (9422) 32 pp
US 5366986 A 941122 (9501) 48 pp
ADT WO 9210096 A1 WO 91-US9303 911206; AU 9191274 A AU 91-91274 911206, WO 91-US9303 911206; EP 561989 A1 WO 91-US9303 911206, EP 92-902227 911206; JP 06503829 W WO 91-US9303 911206, JP 92-502730 911206; US 5366986 A CIP of US 88-182275 880415, US 90-623849 901206
FDT AU 9191274 A Based on WO 9210096; EP 561989 A1 Based on WO 9210096; JP 06503829 W Based on WO 9210096; US 5366986 A CIP of US 5173499
PRAI US 90-623849 901206
AB WO 9210096 A UPAB: 950524
Spiro-Benzodihydrofuran-2 (3H)-cyclohexane derivs. of formula (I), their salts with acids and bases, and esters, are new.

In (I) R = H, 1-4C alkyl, benzyl, or phenyl (all opt. substd); R1, R2 = COOH, CHO, CH2OH, N-(1-4C alkyl) carbamoyl, CF3, halo, vinyl (and substd. vinyl up to 10C), upto 20C alkylidene, aliphatic or aromatic acyl (both opt. substd.), sulphomoyl, aminomethyl, mono- and di- (1-4C alkyl) aminomethyl; a heterocyclic ring, N-acylcarbamoyl, amidine, or hydrazide; or R1 R2 together with their attached C atoms = a cyclic anhydride or lactone.

USE - (I) inhibit complement and/or possess immunosuppressive activity. They are used in treatment of soft tissue distruction due to bearer, myocardial infarct induced trauma, adult respiratory distress syndrome (ARDS), myocardial ischaemia and reperfusion, specific and non-specific proteolytic processing of C5, inflammation due to kidney stones, systemic lupus erythematosis, reptro toxic glomerulopepiciter, multiple sclerosis, atropsic gastrities, thyroidetis, allergic encephalomyelitis, gastric mucosa, thyrotoxicosis, autoimmune haemolytic anaemia, permpligus vulgaris, sympathetic ophthalmia, delayed type hypersensitivity, autoimmune disorders and drug allergies, and in plasminogen activator therapy and cardiopulmonary by-pass. (I) are also used in the treatment of patients with graft rejection, graft-host rejection, or organ transplant rejection, whether xenograft or allograft, e.g. for heart transplants.

0/8

Dwg.0/8

L28 ANSWER 1 OF 1 COPYRIGHT 1995 DERWENT INFORMATION LTD
AN 88-309300 [44] WPIDS
CR 89-087521 [12]; 91-327155 [45]
DNC C88-136776
TI New 13,14-di hydro-15-oxo-prostaglandin F derivs. - useful as vasopressors which raise blood pressure without transient vaso relaxation.
DC B03 B05 C02 C03
IN ODA, T; UENO, R; ITAMI; ODA
PA (RTEC-N) R-TEC UENO LTD; (RTEC-N) R-TECH UENO LTD; (UENS) UENO SEIYAKU OYO KENKYUSHO KK; (RTEC-N) R-TECH UENO CO LTD
CYC 25
PI EP 289349 A 881102 (8844)* EN 69 pp
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
ZA 8806909 A 890530 (8928)
JP 01151552 A 890614 (8930)
ZA 8806872 A 890530 (8935)
GB 2225573 A 900606 (9023)#
EP 289349 B 920129 (9205)
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
DE 3868127 G 920312 (9212)
US 5106869 A 920421 (9219) 51 pp

ES 2032016 T3 930101 (9305)
US 5212200 A 930518 (9321) 15 pp
US 5221763 A 930622 (9326) 51 pp
JP 05071567 B 931007 (9343) 19 pp
CA 1324129 C 931109 (9351)
KR 9300051 B1 930106 (9415)
JP 06080571 A 940322 (9416) 16 pp
CA 1328075 C 940329 (9418)
KR 9306202 B1 930708 (9426)
JP 06067900 B2 940831 (9433) 60 pp

ADT EP 289349 A EP 88-303931 880429; JP 01151552 A JP 88-108329 880430; ZA 8806872 A ZA 88-6872 880915; GB 2225573 A GB 88-21817 880916; US 5106869 A US 90-579116 900907; ES 2032016 T3 EP 88-303931 880429; US 5212200 A Cont of US 88-246059 880919, Div ex US 90-584669 900919, US 91-760280 910916; US 5221763 A Cont of US 88-189100 880502, Cont of US 90-607791 901031, US 92-945594 920916; JP 05071567 B JP 88-230469 880914; CA 1324129 C CA 88-565406 880428; KR 9300051 B1 KR 88-12030 880916; JP 06080571 A Div ex JP 88-230469 880914, JP 93-24099 880914; CA 1328075 C CA 88-577220 880913; KR 9306202 B1 KR 88-4998 880430; JP 06067900 B2 JP 88-108329 880430

FDT ES 2032016 T3 Based on EP 289349; US 5212200 A Cont of US 5001153, Div ex US 5151444; JP 05071567 B Based on JP 02000108; JP 06067900 B2 Based on JP 01151552

PRAI JP 87-107529 870430; JP 87-235890 870918; JP 87-334037 871229; JP 87-108329 870430; US 87-97988 870917

AB EP 289349 A UPAB: 940608

13,14-Dihydro-15-oxo-PGF derivs. of formula (I) and their salts are new, where X=(CH2)3, CH2,COCH2, cis-CH2CH=CH or CH2C triple C; R1=H, 1-4C alkyl, phenyl, benzoyl, hydroxyalkyl, alkoxyalkyl, trialkylsilyl or tetrahydropyranyl; R2=H or lower alkyl; R3 and R'3=OH, Me or CH2OH; R4 and R5=H, halogen or lower alkyl; R6=4-9C alkyl (opt. contg. a double bond or substd. by alkoxy) or YAr; Ar=phenyl opt. monosubstd. by halogen or haloalkyl; Y=a bond or O; except for cpds. where R1=R2=R4=R5=H, R6=n=Bu, R3=R'3=alpha-OH and the 2,3 posn. is singly bonded.

USE/ADVANTAGE - (I) are vasopressors which raise blood pressure without transient vasorelaxation and with little or no tracheal, bronchial or intestinal contraction effects. They may be used to treat humans or animals.

Dwg.0/2

=> fil medl
FILE 'MEDLINE' ENTERED AT 10:45:37 ON 29 JUN 95

FILE LAST UPDATED: 21 JUN 1995 (950621/UP). FILE COVERS 1966 TO DATE.
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MEDLINE, CANCERLIT AND PDQ ERRONEOUSLY ANNOTATED CERTAIN ARTICLES AUTHORED OR CO-AUTHORED BY DR. BERNARD FISHER WITH THE PHRASE

"SCIENTIFIC MISCONDUCT-DATA TO BE REANALYZED." ALL SUCH ANNOTATIONS HAVE BEEN REMOVED OR ARE BEING REMOVED. WE APOLOGIZE FOR ANY PROBLEMS OR CONCERNS THIS MAY HAVE CAUSED. USERS SHOULD DISREGARD THOSE PRIOR ANNOTATIONS.

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                DEL HIS Y
L1            70 S C5 (L) (NEPHRITIS OR GLOMERULONEPH?)
L2          2169 S (COMPLEMENT 5+NT)/CT
                E NEPHRITIS/CT
                E E3+ALL
L3         33825 S NEPHRITIS+NT/CT
L4            69 S L3 AND L2
L5            28 S ANTIBOD? AND L4
L6             0 S L5 AND MONCLONAL?
L7             2 S L5 AND MONOCLONAL?
L8             1 S C5A (L) CLEAVAGE SITE#
L9            26 S L5 NOT L7
L10            0 S 5G46# OR 5G27# OR 5G200## OR KSSKC
L11            0 S 5G325#
L12            0 S C5G46# OR CD5G27# OR C5G200## OR KSSKC
L13            0 S C5 G46# OR CD5 VG27# OR C5 G200## OR KSSKC
L14            0 S C5 G46# OR C5 VG27# OR C5 G200## OR KSSKC

     FILE 'MEDLINE' ENTERED AT 10:45:37 ON 29 JUN 95

=> d bib ab l7 1-2;l bib ab l8;d bib ab l9 1-6

L7   ANSWER 1 OF 2  MEDLINE
AN   90314446     MEDLINE
TI   Membrane attack complex of complement in Henoch-Schonlein purpura
     skin and nephritis.
AU   Kawana S; Shen G H; Kobayashi Y; Nishiyama S
CS   Department of Dermatology, Kitasato University School of Medicine,
     Kanagawa, Japan.
SO   Arch Dermatol Res, (1990) 282 (3) 183-7.
     Journal code: 6X7. ISSN: 0340-3696.
CY   GERMANY, WEST: Germany, Federal Republic of
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   9010
AB   The present study using direct immunofluorescence with
   monoclonal antibodies to C5b-9 complex-related
     antigens was undertaken to determine whether complement activation
     in Henoch-Schonlein purpura (HSP) causes assembly of the membrane
     attack complex of complement (MAC) in skin and nephritis lesions.
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The deposition of C5, C6, C7, C8, C9, and C5b-9 neoantigens was noted in the vascular walls of papillary dermis and/or subpapillary dermal plexus of the vessels in 11 out of 15 patients with HSP. Their presence in vessel walls indicates complement activation which leads to terminal complement activation. There were small deposits of S protein at the same sites in three of the 11 skin specimens. Thus, the majority of C5b-9 demonstrated in HSP skin was the cytolytically active C5b-9 complex, MAC. Granular deposits of C5b-9 related antigens without S protein were also found in the capillary walls and mesangium of the glomeruli of two out of four specimens from patients with HSP nephritis; in the other two S protein was colocalized with the deposition of C5b-9. The results of the present study indicate that complement activation leading to generation of MAC may possibly be involved in the pathogenesis of vascular injury in a significantly large number of skin lesions and of HSP nephritis.

L7 ANSWER 2 OF 2 MEDLINE
AN 88257455 MEDLINE
TI SP-40,40, a newly identified normal human serum protein found in the SC5b-9 complex of complement and in the immune deposits in glomerulonephritis.
AU Murphy B F; Kirszbaum L; Walker I D; d'Apice A J
CS Department of Nephrology, Royal Melbourne Hospital, Australia.
SO J Clin Invest, (1988 Jun) 81 (6) 1858-64.
Journal code: HS7. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 8810
AB We report herein the isolation and initial characterization of a novel protein, termed SP-40,40, which is present at moderate levels (35-105 micrograms/ml) in normal human serum. SP-40,40 is deposited in the renal glomeruli of patients with glomerulonephritis but is not found in normal glomeruli. The protein is a heterodimeric structure of relative molecular mass 80 kD, both chains of which are of a similar size (40 kD). The amino-terminal sequences of both chains are unrelated to one another and possess no significant homology to any known protein sequence. The tissue distribution of SP-40,40 closely resembles that of the terminal complement components and its physicochemical properties are similar to, but distinct from, those of the S protein of complement. We have identified SP-40,40 in the SC5b-9 complex of complement and have demonstrated incorporation of labeled SP-40,40 into this complex. These data suggest that SP-40,40 is an additional component of SC5b-9.

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=> d bib ab l8;d bib ab l9 1-26

L8 ANSWER 1 OF 1 MEDLINE
AN 93084373 MEDLINE
TI Streptococcal C5a peptidase is a highly specific endopeptidase.
AU Cleary P P; Prahbu U; Dale J B; Wexler D E; Handley J
CS Department of Microbiology, University of Minnesota, Minneapolis 55455.
NC AI20016 (NIAID)
SO Infect Immun, (1992 Dec) 60 (12) 5219-23.
Journal code: GO7. ISSN: 0019-9567.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9303
AB Compositional analysis of streptococcal **C5a** peptidase (SCPA) cleavage products from a synthetic peptide corresponding to the 20 C-terminal residues of **C5a** demonstrated that the target **cleavage site** is His-Lys rather than Lys-Asp, as previously suggested. A **C5a** peptide analog with Lys replaced by Gln was also subject to cleavage by SCPA. This confirmed that His-Lys rather than Lys-Asp is the scissile bond. Cleavage at histidine is unusual but is the same as that suggested for a peptidase produced by group B streptococci. Native C5 protein was also resistant to SCPA, suggesting that the His-Lys bond is inaccessible prior to proteolytic cleavage by C5 convertase. These experiments showed that the streptococcal **C5a** peptidase is highly specific for **C5a** and suggest that its function is not merely to process protein for metabolic consumption but to act primarily to eliminate this chemotactic signal from inflammatory foci.

L9 ANSWER 1 OF 26 MEDLINE
AN 92261749 MEDLINE
TI Acute effect of passive Heymann nephritis on renal blood flow and glomerular filtration rate in the rat: role of the anaphylatoxin C5a and the alpha-adrenergic nervous system.
AU Sekse I; Iversen B M; Daha M R; Ofstad J
CS Renal Research Group, University of Bergen, Haukeland University Hospital, Norway.
SO Nephron, (1992) 60 (4) 453-9.

Journal code: NW8. ISSN: 0028-2766.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9208
AB In earlier studies, we have shown that induction of passive Heymann nephritis (PHN) by intrarenal infusion of anti-Fx1A **antibodies** provokes an immediate fall in renal blood flow (RBF) and glomerular filtration rate (GFR). This was probably mediated via the complement system, as infusion of the F(ab')2 fraction of anti-Fx1A did not reduce RBF and GFR. In the present study, the effects of alpha-adrenergic blockade upon the acute hemodynamic changes during induction of PHN and of C5a infusion were studied. Group 1 was infused with anti-Fx1A **antibodies** during blockade of the sympathetic nervous system with the alpha-blocker phentolamine; control animals were treated similarly, but infused with normal rat IgG. Group 2 was infused with the anaphylatoxin C5a, normally produced during complement activation, and compared with control animals infused with saline. In group 1, RBF did not differ from control animals after the infusion of anti-Fx1A **antibodies** (6.6 +/- 0.5 compared to 7.3 +/- 1.0 ml/min/g in the controls). GFR in the left, **antibody** -infused kidney fell compared to controls, and was 0.25 +/- 0.08 ml/min/g at the end of the experiment compared to 0.60 +/- 0.13 ml/min/g (p less than 0.05 with Student's t test, p = 0.07 with two-way analysis of variance (ANOVA). GFR in the right kidney remained unchanged compared to controls. In group 2, C5a induced a significant fall in RBF (from 7.9 +/- 0.9 to 3.1 +/- 0.4 ml/min/g kidney weight), significantly different from control animals where it fell from 8.1 +/- 0.5 to 6.8 +/- 0.7 ml/min/g (p less than 0.0001 with two-way ANOVA, p less than 0.001 with t test).(ABSTRACT TRUNCATED AT 250 WORDS)

L9 ANSWER 2 OF 26 MEDLINE
AN 90379201 MEDLINE
TI Patterns of complement activation in idiopathic membranoproliferative glomerulonephritis, types I, II, and III.
AU Varade W S; Forristal J; West C D
CS Children's Hospital Research Foundation, Cincinnati, OH.
SO Am J Kidney Dis, (1990 Sep) 16 (3) 196-206.
Journal code: 3H5. ISSN: 0272-6386.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 9012
AB Complement profiles on 22 hypocomplementemic patients with membranoproliferative glomerulonephritis (MPGN) type I, on 11 with

MPGN II, and on 16 with MPGN III, gave evidence that the nephritic factor of the amplification loop (NFa) is responsible for the hypocomplementemia in MPGN II and the nephritic factor of the terminal pathway (NFt) for the hypocomplementemia in MPGN III. In contrast, in MPGN I, there was evidence for three complement-activating modalities, NFa, NFt, and immune complexes. As a result, four different patterns of complement activation were seen. NFa, found in MPGN II, produces a complement profile characterized mainly by C3 depression. In addition, four of seven (57%) severely hypocomplementemic MPGN II patients (C3 less than 30 mg/dL) had slightly depressed levels of factor B, and one of seven (14%) of properdin, but in all the C5 concentration was normal. In contrast, all eight severely hypocomplementemic patients with MPGN II had depressed C5 and properdin levels, and six of eight (75%) depressed levels of C6, C7, and/or C9. Of eight MPGN III patients with moderate hypocomplementemia, 50% had depressed C5 and properdin levels and the remainder, depressed C3 only. This spectrum of profiles is most likely produced by varying concentrations of NFt. In MPGN I, nine of 23 (39%) had a profile indicating only classical pathway activation; seven of 23 (39%), a pattern compatible with NFt alone; four of 23 (9%), evidence for both classical pathway activation and NFt; and three of 23 (13%), a pattern compatible with NFa. The unique multifactorial origin of the hypocomplementemia in MPGN I, often giving evidence of classical pathway activation, together with previously reported differences in glomerular morphology and clinical features at onset, makes it distinct from MPGN III. Depressed C8 levels were found to some extent in all hypocomplementemic states. The levels were uncommonly depressed in patients with NFa, most markedly depressed with NFt, and moderately reduced with classical pathway activation. The cause is not known. Diagnostically, profiles showing classical pathway activation and low levels of C6, C7, and/or C9 are specific for MPGN I. Those showing only classical activation are likewise diagnostic of MPGN I if systemic lupus erythematosus (SLE) and chronic bacteremia are ruled out.

L9 ANSWER 3 OF 26 MEDLINE
AN 90348132 MEDLINE
TI Anti-GBM nephritis in the mouse: role of granulocytes in the heterologous phase.
AU Schrijver G; Bogman M J; Assmann K J; de Waal R M; Robben H C; van Gasteren H; Koene R A
CS Department of Pathology, University Hospital Nijmegen, The Netherlands.
SO Kidney Int, (1990 Jul) 38 (1) 86-95.
Journal code: KVB. ISSN: 0085-2538.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
EM 9011
AB The role of polymorphonuclear granulocytes (PMNs) was studied in a model of anti-GBM nephritis in mice, in which PMN depletion was induced by total body irradiation of 7.5 Gy. Both in complement-normal B10.D2 new and in C5-deficient B10.D2 old mice, PMN depletion completely prevented the albuminuria occurring after injection of low doses of anti-GBM serum, and severely depressed the albuminuria after injection of high doses. In immunofluorescence, glomerular deposition of **antibody** and C3 was similar to that in control mice. The glomerular influx of PMNs in both the complement-normal and C5-deficient controls was inhibited to 10% or less of control values. Fibrin deposition or necrosis did not occur. Injection of F(ab')2 fragments of the anti-GBM **antibody** in non-irradiated mice caused only limited PMN influx and reduced the albuminuria to physiological levels, although the binding of 125I labeled F(ab')2 fragments to the glomeruli was as high as 82% of that of the complete **antibody**. We conclude that the albuminuria in this model is Fc-dependent and largely, if not completely, dependent on the influx of PMNs in the glomeruli. Among the many experimental models of anti-GBM nephritis, this is the first one in which the heterologous phase is complement-independent but PMN-dependent.

L9 ANSWER 4 OF 26 MEDLINE
AN 89035829 MEDLINE
TI Hydroxyl radical scavengers ameliorate proteinuria in rat immune complex glomerulonephritis.
AU Rahman M A; Emancipator S S; Sedor J R
CS Department of Medicine, Case Western Reserve University, Cleveland, Ohio.
NC DK 38544
SO J Lab Clin Med, (1988 Nov) 112 (5) 619-26.
Journal code: IVR. ISSN: 0022-2143.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 8902
AB We examined the effect of the administration of different oxygen radical scavengers on the development of glomerulonephritis induced by cationic bovine gamma-globulin (cBGG). Treatment with the H2O2 scavenger catalase or the superoxide anion (O2-) scavenger superoxide dismutase (SOD) did not significantly reduce proteinuria. In contrast, treatment with the hydroxyl radical (OH.) scavengers dimethyl sulfoxide (DMSO) or dimethylthiourea resulted in significant decrements in proteinuria, from 156 +/- 20 mg/24 hours in saline solution--treated control rats to 70 +/- 17 mg/24 hours (p less than 0.05) and 37 +/- 10 mg/24 hours (p less than 0.01) in

DMSO- and dimethylthiourea-treated rats, respectively. Therapy with DMSO for 5 days after induction of glomerular disease also resulted in amelioration of proteinuria, 10.0 +/- 5.0 mg/24 hours versus saline solution-treated rats, 67.6 +/- 16.2 mg/24 hours (p less than 0.005). OH. scavenger therapy did not influence glomerular morphology, glomerular immunoglobulin G (IgG), or complement deposition, or creatinine clearances of rats with glomerulonephritis. Furthermore, there were no significant differences in serum levels of C3 and C5 or anti-BGG **antibody** production between DMSO-treated rats and control rats. None of the radical scavengers administered altered the enhanced glomerular thromboxane synthesis characteristic of this model. Our results suggest that OH. generation mediates in part glomerular injury in cBGG-induced glomerulonephritis.

L9 ANSWER 5 OF 26 MEDLINE
AN 89012949 MEDLINE
TI Antiglomerular basement membrane nephritis in the mouse. Study on the role of complement in the heterologous phase.
AU Schrijver G; Assmann K J; Bogman M J; Robben J C; de Waal R M; Koene R A
CS Department of Pathology, University Hospital Nijmegen, The Netherlands.
SO Lab Invest, (1988 Oct) 59 (4) 484-91.
Journal code: KZ4. ISSN: 0023-6837.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8901
AB The role of complement was examined in a model of antiglomerular basement membrane nephritis in the mouse, induced by intravenous injection of goat anti-mouse glomerular basement membrane serum, and characterized by early glomerular lesions and a dose-dependent albuminuria. We compared the reaction after injection of the antiserum in complement-normal B10.D2 new mice with that in congenic, congenitally C5-deficient B10.D2 old mice, and in both strains after C3 depletion by treatment with cobra venom factor. The dose-dependent albuminuria was not affected by the absence of complement activation. Also, deficiency of C3 and/or C5 had no inhibitory effect on the histologic glomerular lesions: it did not reduce the influx of polymorphonuclear granulocytes in the glomerular capillary vessels, nor prevented the eventual intravascular coagulation. We conclude that complement-independent mechanisms are involved in the development of the heterologous phase of antiglomerular basement membrane nephritis in the mouse.

L9 ANSWER 6 OF 26 MEDLINE
AN 89012948 MEDLINE

TI Complement and leukocyte independent proteinuria and eicosanoid synthesis in rat membranous nephropathy.

AU Rahman M A; Liu C N; Dunn M J; Emancipator S N
CS Department of Medicine, Hines Veterans Administration Hospital, Illinois.

NC DK 38544
HL 22563
SO Lab Invest, (1988 Oct) 59 (4) 477-83.
Journal code: KZ4. ISSN: 0023-6837.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8901

AB We examined the effect of complement depletion and leukocyte depletion on an experimental model of membranous nephropathy. Nephrosis was induced in 200-gm male Sprague-Dawley rats by priming with cationic bovine gamma-globulin in adjuvant on day 1 followed by intravenous challenge with antigen starting on day 10. No naive control rats had immunofluorescent deposits in glomeruli; urine protein was less than 10 mg/24 hour and glomerular thromboxane synthesis was 658 +/- 64 ng/mg glomerular dry weight. In contrast, all rats primed and challenged with cationic bovine gamma-globulin had intense granular capillary wall deposits of rats IgG, bovine gamma-globulin, C3 and C5; severe proteinuria (183 +/- 24 mg/24 hour) was observed, associated with a 3-fold increase in glomerular thromboxane (2,393 +/- 574 ng/mg, all p less than 0.01 versus naive controls). In some rats, administration of cobra venom factor and antiserum to rat C3, starting on day 8 was used to deplete complement; hemolytic C3 and C5 were less than 2% of normal at sacrifice. These rats had IgG and bovine gamma-globulin deposits, whereas they lacked glomerular C3 or C5. Proteinuria (209 +/- 28 mg/24 hour) and glomerular thromboxane (2,087 +/- 394 ng/mg) were markedly increased compared with control, but no different from normocomplementemic rats primed and challenged with cationic bovine gamma-globulin. In other rats, depletion of leukocytes was achieved by 1,000 R x-irradiation on day 7; at sacrifice, irradiated rats had 1,270 +/- 462 wbc/microliter versus 10,375 +/- 1,652 in nephrotic rats given no other treatment, with unaltered differentials. These rats had glomerular deposits of rat IgG, bovine gamma-globulin, C3 and C5 indistinguishable from nephrotic rats with normal leukocyte counts in intensity and distribution. Proteinuria (202 +/- 30) and glomerular thromboxane (2,358 +/- 189 ng/mg) were markedly elevated compared with naive controls, but were not different from the normocomplementemic or complement-depleted groups primed and challenged with antigen. An additional control group included rats primed with ovalbumin on day 1, irradiated with 1,000 R on day 7, and challenged with cationic bovine gamma-globulin starting on day 10. This group had granular capillary wall deposits of bovine

gamma-globulin, but not deposits of IgG, C3, or C5; urine protein excretion (less than 10 mg/24 hours) and glomerular thromboxane synthesis (613 +/- 90) were not different from naive controls. Glomerular prostaglandin E2 synthesis did not differ among the five groups.(ABSTRACT TRUNCATED AT 400 WORDS)

L9 ANSWER 7 OF 26 MEDLINE
AN 89002349 MEDLINE
TI IgA nephropathy: a clinicopathological study with emphasis on both nephrotic syndrome and complements.
AU Ho Y S; Chen A; Sheu L F; Tu Y C
SO Chung Hua I Hsueh Tsa Chih, (1987 Dec) 40 (6) 523-36.
Journal code: CHQ. ISSN: 0578-1337.
CY TAIWAN: Taiwan, Province of China
DT Journal; Article; (JOURNAL ARTICLE)
LA English
EM 8901

L9 ANSWER 8 OF 26 MEDLINE
AN 88288498 MEDLINE
TI C5 component: immunopathological index for the activity of IgA nephropathy [letter].
AU Chen A; Ho Y S; Tu Y C
SO Nephron, (1988) 49 (3) 255.
Journal code: NW8. ISSN: 0028-2766.
CY Switzerland
DT Letter
LA English
FS Priority Journals
EM 8811

L9 ANSWER 9 OF 26 MEDLINE
AN 88177600 MEDLINE
TI Exacerbating factors in patients with IgA nephropathy.
AU Tomino Y; Sakai H
CS Department of Internal Medicine, School of Medicine, Tokai University, Tokai University, Isehara City, Japan.
SO Semin Nephrol, (1987 Dec) 7 (4) 315-7.
Journal code: SER. ISSN: 0270-9295.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8807

L9 ANSWER 10 OF 26 MEDLINE
AN 88177593 MEDLINE
TI The role of IgG, IgM, and C3 in experimental murine IgA nephropathy.
AU Emancipator S N; Lamm M E

CS Institute of Pathology, Case Western Reserve University, Cleveland, OH 44106.
NC DK 38544
CA 32582
SO Semin Nephrol, (1987 Dec) 7 (4) 286-8.
Journal code: SER. ISSN: 0270-9295.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8807

L9 ANSWER 11 OF 26 MEDLINE
AN 88156140 MEDLINE
TI C3 dependent, C5 independent immune complex glomerulopathy in the mouse.
AU Sawtell N M; Hartman A L; Weiss M A; Pesce A J; Michael J G
CS Department of Pathology, University of Cincinnati Medical Center, Ohio.
NC AI-15520
SO Lab Invest, (1988 Mar) 58 (3) 287-93.
Journal code: KZ4. ISSN: 0023-6837.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8806
AB This study examines the role of complement in a murine model of accelerated nonproliferative immune complex glomerulopathy. Two C5 deficient strains (DBA/2J and B10.D2oSnJ) as well as normocomplementemic mice consistently develop heavy proteinuria and glomeruli show loss of normal visceral epithelial cell architecture within 4 days of intravenous antigen administration. In contrast, animals depleted of C3 with cobra venom factor fail to develop proteinuria and retain discrete foot processes. Semiquantitative evaluation of antigen and **antibody** in glomeruli shows equivalent deposition in mice from all groups. The localization of these deposits, however, is different in C3-depleted mice. There is extensive accumulation of deposits along the subepithelial aspect of the glomerular basement membrane of normocomplementemic and C5 deficient mice while deposits in glomeruli of C3-depleted animals accumulate in the subendothelial region and do not cross the glomerular basement membrane. These data demonstrate that in this model, glomerular injury is dependent on complement components generated up thru C3 but not C5 or latter components. In addition, our data suggest that C3 is important in the movement of immune complexes across the glomerular basement membrane. Although the mechanism by which complement is mediating injury in this model is not known, it does not appear to involve an inflammatory cell

infiltrate or the terminal complement components.

L9 ANSWER 12 OF 26 MEDLINE
AN 88130355 MEDLINE
TI Glomerular hemodynamics in experimental glomerulonephritis.
AU Blantz R C; Gabbai F B; Wilson C B
CS Nephrology-Hypertension Section, Veterans Administration Medical Center, San Diego, California.
SO Adv Nephrol Necker Hosp, (1988) 17 3-13. Ref: 37
Journal code: 2NV. ISSN: 0084-5957.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 8805

L9 ANSWER 13 OF 26 MEDLINE
AN 87302421 MEDLINE
TI Effect of the anticomplementary agent, K-76 monocarboxylic acid, on experimental immune complex glomerulonephritis in rats.
AU Iida H; Izumino K; Asaka M; Takata M; Mizumura Y; Sasayama S
SO Clin Exp Immunol, (1987 Jan) 67 (1) 130-4.
Journal code: DD7. ISSN: 0009-9104.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 8712
AB We examined the effect of the anticomplementary agent K-76 monocarboxylic acid (K-76COOH), which is known to inhibit C5 activity, on immune complex glomerulonephritis in rats. Bovine serum albumin (BSA) nephritis was induced in rats by subcutaneous immunization and daily intravenous administration of BSA. K-76COOH (30 mg/kg) was administered intraperitoneally twice daily for 4 weeks. It was shown that K-76COOH would significantly reduce the development of proteinuria in the early stage of BSA nephritis, but it failed to suppress proteinuria in the late stage. There was no significant difference in glomerular changes between treated animals and non-treated controls. These findings suggest that C5, and the terminal complement components may play a significant role in protein excretion in the early stage of immune complex glomerulonephritis.

L9 ANSWER 14 OF 26 MEDLINE
AN 87062068 MEDLINE
TI Immune complex induced glomerular lesions in C5 sufficient and deficient mice.

AU Falk R J; Jennette J C
NC AM34855-01
AM30701-04
SO Kidney Int, (1986 Nov) 30 (5) 678-86.
Journal code: KVB. ISSN: 0085-2538.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8703
AB The role in the pathogenesis of immune complex-mediated glomerulonephritis of C5 or some terminal complement component dependent upon C5 for activation was explored in a congenic strain of C5 sufficient (NSN) and C5 deficient (OSN) mice. When these mice were given daily injections of heterologous protein, horse apoferritin (HAF), there were profound differences between the strains in the development of glomerulonephritis and renal dysfunction. When NSN and OSN mice produced low levels of anti-HAF, NSN mice developed extensive glomerular deposits of HAF and immune reactants and a mild proliferative glomerulonephritis. In contrast, comparable OSN mice developed only trace mesangial localization of HAF and no glomerular lesions by light microscopy. When NSN and OSN mice produced high levels of anti-HAF, both strains had equivalent glomerular immune deposits; however, NSN mice developed a severe necrotizing and crescentic glomerulonephritis, while OSN mice had much less glomerular injury. Compared to OSN mice, these NSN mice also had much more severe tubulointerstitial injury, and significantly higher serum creatinine levels. Thus, in this experimental model, the absence of C5 resulted in reduced glomerular immune complex localization when there were small amounts of circulating immune reactants; and in markedly reduced glomerular leukocyte influx, necrosis and crescent formation, when large amounts of immune reactants have localized in glomeruli. These effects could be mediated by C5 (such as C5a) or by some terminal complement component(s) dependent upon C5 for activation.

L9 ANSWER 15 OF 26 MEDLINE
AN 85186248 MEDLINE
TI Detection of terminal complement components in experimental immune glomerular injury.
AU Adler S; Baker P J; Pritzl P; Couser W G
NC AM-17722
AM-32051
AM-32082
SO Kidney Int, (1984 Dec) 26 (6) 830-7.
Journal code: KVB. ISSN: 0085-2538.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English

FS Priority Journals
EM 8508
AB Complement mediates glomerulonephritis by inflammatory cell-dependent and non-inflammatory cell-independent effects on glomerular permeability. The latter may involve terminal components of the complement system. We examined several models of immunologic renal injury in the rat by immunofluorescence (IF) for terminal complement components C5, C6, C7, and C8 in glomeruli using antisera to human C5-8, which cross-react with the analogous rat complement components. Rats with the heterologous and autologous phases of passive Heymann nephritis (PHN) had proteinuria and 1 to 2+ capillary wall deposits of heterologous or rat IgG, rat C3, and C5-8. Complement depletion with cobra venom factor (CVF) significantly decreased proteinuria in both models and prevented deposition of all complement components. Rats with active Heymann nephritis had similar deposits of rat IgG and C5-8. Rats with anti-GBM nephritis and aminonucleoside nephrosis had severe proteinuria which was not affected by CVF treatment and deposits of C5-8 were absent. The presence of terminal complement components in immune deposits in experimental glomerular disease correlates with a functional role for complement in mediating glomerular injury. These data support the hypothesis that the terminal complement pathway may be a major mediator of some types of immune glomerular injury.

L9 ANSWER 16 OF 26 MEDLINE
AN 84062259 MEDLINE
TI Role of the terminal complement pathway in experimental membranous nephropathy in the rabbit.
AU Groggel G C; Adler S; Rennke H G; Couser W G; Salant D J
NC AM 00742
AM 07053
AM 17722
+
SO J Clin Invest, (1983 Dec) 72 (6) 1948-57.
Journal code: HS7. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 8403
AB Our recent observations of a complement-mediated, cell-independent mechanism of altered glomerular permeability in rat membranous nephropathy suggested a possible role for the terminal complement pathway in the mediation of proteinuria in certain forms of glomerular disease. To directly determine whether the membranolytic terminal complement components (C5b-C9) are involved in glomerular injury, we studied the development of proteinuria in normal and C6-deficient (C6D) rabbits, in both of which a membranous nephropathy-like lesion develops early in the course of immunization

with cationized bovine serum albumin (cBSA) (pI 8.9-9.2). C6 hemolytic activity of C6D was 0.01% that of control rabbits. After 1 wk of daily intravenous injections of cBSA, proteinuria developed in 71% of controls (median 154, range 1-3,010 mg/24 h, n = 24), whereas none of C6D were proteinuric (median 6, range 2-12 mg/24 h, n = 12, P less than 0.01). After 1 wk of cBSA, both groups had qualitatively identical glomerular deposits of BSA, rabbit IgG, and C3 on immunofluorescence microscopy, predominantly subepithelial electron-dense deposits on electron microscopy, and minimal glomerular inflammatory cell infiltration of glomeruli. Glomeruli were isolated from individual animals after 1 wk of cBSA and deposits of rabbit IgG **antibody** were quantitated by a standardized in vitro assay using anti-rabbit IgG-125I. Rabbit IgG deposits were found to be similar in control (29.8 +/- 13.2, range 12.7-48.6 micrograms anti-IgG/2,000 glomeruli, n = 6) and C6D rabbits (32.6 +/- 13.8, range 16.8-48.8 micrograms anti-IgG/2,000 glomeruli, n = 5, P greater than 0.05). After 2 wk, coincident with a prominent influx of mononuclear cells and neutrophils, proteinuria developed in C6D rabbits. These results document, for the first time, a requirement for a terminal complement component in the development of immunologic glomerular injury. Since the only known action of C6 is in the assembly of the membrane attack complex, these observations suggest that the membranolytic properties of complement may contribute to glomerular damage.

L9 ANSWER 17 OF 26 MEDLINE
AN 83280836 MEDLINE
TI Diagnostic tests and clinical subsets in systemic lupus erythematosus: update 1983.
AU Weiss R A; Mogavero H S Jr; Synkowski D R; Provost T T
SO Ann Allergy, (1983 Aug) 51 (2 Pt 1) 135-46. Ref: 94
Journal code: 4XC. ISSN: 0003-4738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 8311

L9 ANSWER 18 OF 26 MEDLINE
AN 82126464 MEDLINE
TI Complement mediated inflammatory reactions.
AU Kunkel S L; Fantone J C 3d; Ward P A
SO Pathobiol Annu, (1981) 11 127-54. Ref: 127
Journal code: ORW.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English

FS Priority Journals
EM 8206

L9 ANSWER 19 OF 26 MEDLINE
AN 82089534 MEDLINE
TI Immune complex injury of the lung. Symposium held at the 74th annual meeting of the American Thoracic Society, Las Vegas, Nevada, May 1979.
AU Daniele R P; Henson P M; Fantone J C 3d; Ward P A; Dreisin R B
NC HL-23877
HL-21565
AI-09651
+
SO Am Rev Respir Dis, (1981 Dec) 124 (6) 738-55. Ref: 185
Journal code: 426. ISSN: 0003-0805.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 8204

L9 ANSWER 20 OF 26 MEDLINE
AN 81125856 MEDLINE
TI Complement activation in acute glomerulonephritis in children.
AU Levy M; Sich M; Pirotzky E; Habib R
SO Ric Clin Lab, (1980 Jan-Mar) 10 (1) 87-91.
Journal code: TEA. ISSN: 0390-5748.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8106

L9 ANSWER 21 OF 26 MEDLINE
AN 81005532 MEDLINE
TI Immunohistological studies in IgA nephropathy (author's transl).
AU Tomino Y
SO Hokkaido Igaku Zasshi, (1980 Mar) 55 (2) 123-30.
Journal code: GA9.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA Japanese
FS Priority Journals
EM 8101

L9 ANSWER 22 OF 26 MEDLINE
AN 80135380 MEDLINE
TI The biological role of the complement system and the clinical

importance of complement measurements.
AU Fust G
SO Haematologia (Budap), (1978-79) 12 (1-4) 85-106. Ref: 38
Journal code: FY5. ISSN: 0017-6559.
CY Hungary
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 8007
AB Properties of serum proteins belonging to the complement system, two pathways of the complement activation (classical and alternative pathway) as well as the physiological role of the complement system are discussed. Complement has essential importance in some physiological processes: In the induction of the humoral immune response, in the elimination of immune complexes and in the protection against bacterial and viral infections. After a short discussion of the genetics of the complement system, the principle and possibilities of clinical applications of the complement measurements are described. Finally, different approaches to the therapeutic manipulation of the complement system are discussed.

L9 ANSWER 23 OF 26 MEDLINE
AN 79002509 MEDLINE
TI Immunopathology of membranoproliferative glomerulonephritis with subendothelial deposits (Type I MPGN).
AU Levy M; Gubler M C; Sich M; Beziau A; Habib R
SO Clin Immunol Immunopathol, (1978 Aug) 10 (4) 477-92.
Journal code: DEA. ISSN: 0090-1229.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 7901

L9 ANSWER 24 OF 26 MEDLINE
AN 77054623 MEDLINE
TI Nephritic factor: Description of a new quantitative assay and findings in glomerulonephritis.
AU Border W A; Wilson C B; Gotze O
SO Kidney Int, (1976 Oct) 10 (4) 311-8.
Journal code: KVB. ISSN: 0085-2538.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 7703
AB A sensitive quantitative test for nephritic factor (NF) in human serum is reported. The test is based on the capacity of NF to

initiate fluid phase consumption of the third complement (C) component in the presence of magnesium ions (Mg++) and of factors of the alternative pathway of C activation. These factors as well as C3 and C5 were supplied by the incorporation of normal human serum (NHS) into the assay mixture. In order to prevent C3 (and C5) consumption via the Ca++- and Mg++-dependent classical pathway, the test was performed in the presence of the chelating agent Mg-ethylene bis (oxyethylene-nitrilo) tetraacetic acid (Mg EGTA) which interacts preferentially with Ca++. The Mg EGTA concentration was found to be critical, a final concentration of 5 mM in the assay mixture being required for optimal results. By its heat stability (54 degrees to 56 degrees C, 30 min), NF could be distinguished from other, heat-labile NF-like factors. The NF test was applied to five categories of patients with glomerulonephritis (GN). Heat-stable NF activity was found in seven of 17 sera in the membranoproliferative glomerulonephritis (MPGN) group. Two of the 12 acute poststreptococcal GN sera had NF-like activity which disappeared upon heating. Serum C3 and proactivator (PA) concentrations varied widely in all groups but a clear positive relationship was found between the presence of NF and low serum C3 concentrations in MPGN. Renal immunofluorescence in MPGN indicated a lesser amount of lg deposited in glomeruli from patients with NF when compared to the NF-negative patients. Both groups had heavy C3 deposits. The availability of a sensitive, quantitative assay for NF may help to provide further insight into the various pathogenic mechanisms in different forms of MPGN.

L9 ANSWER 25 OF 26 MEDLINE
AN 76241436 MEDLINE
TI Classical complement pathway activation in membranoproliferative glomerulonephritis.
AU Ooi Y M; Vallota E H; West C D
SO Kidney Int, (1976 Jan) 9 (1) 46-53.
Journal code: KVB. ISSN: 0085-2538.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 7611
AB Levels of components of the classical and alternative complement pathways and the activity of the C3 nephritic factor (C3NeF) were measured in serum specimens from patients with type I (subendothelial deposits) and type II (intramembranous dense deposits) membranoproliferative glomerulonephritis (MPGN) and the results compared with the levels in normal subjects. Although C3 and C5 concentrations were comparably depressed in type I and type II, the levels of Clq and C4 were lower in type I and the correlation coefficients between Clq vs. C4 and C4 vs. C3 were higher than in type II. The profile was highly suggestive of classical pathway

activation. In contrast, in type II MPGN, factor B levels were lower and C3NeF activity was more frequently detectable and higher. A feature of interest was that type I, as compared to type II, was characterized by significantly lower serum concentrations of properdin, higher and more significant correlation coefficients between serum properdin concentrations and those of Clq, C4 and C3, and consistent glomerular deposition of properdin. The involvement of properdin in type I may reflect recruitment of a pathway resembling the C1 bypass mechanism, said to involve C1, properdin, factor B and C3-9.

L9 ANSWER 26 OF 26 MEDLINE
AN 76157672 MEDLINE
TI The complement system and nephritis.
AU Muller-Eberhard H J
SO Adv Nephrol Necker Hosp, (1974) 4 3-14. Ref: 43
Journal code: 2NV.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 7607